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# WILD ANACARDIACEAE TREES OF ISRAEL AND PALESTINE – COLOR, TASTE, MEDICINE AND UNIQUE CHEMISTRY

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#### **ABSTRACT**

The Anacardiaceae family is represented in the reviewed region by eight species, where one of them is of Brazilian origins. But despite this small number, these trees are among the most colorful, spice sources and with outstanding medicinal activities. The diversity of the known natural products that were isolated from these plants, is very large. This review is the most comprehensive that was ever published about these species in particular, and about the Anacardiaceae in general. The extensive ethnobotanical uses of these trees will be presented in the introduction of this article, followed by a summary of the published modern research publications about these eight trees. Due to great number of chemical compositions publications of these plants, we limited our presentation to carefully selected and limited

number of natural products structures, that will be presented in several figures. An extensive discussion section will follow the presentation of modern research findings, and the article will end with very selected presentation of some activities of three domesticated species of this family. Most of the properties and activities will be presented in tables, for the convenience of readers.

**KEYWORDS**: chemical composition, plant extract, antimicrobial, antioxidant, nutrition, essential oil, Sumac, *Pistacia*, ethnomedicine, *Rhus*.

**Abbreviations**: ABTS 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid), ahc and her/his colleagues, AChE acetylcholine esterase, BHA butylated hydroxyanisole, BHT butylhydroxytoluene, BuChE butyrylcholine esterase, CUPRAC cupric reducing antioxidant capacity, DPPH 2,2-Diphenyl-1-picrylhydrazyl, DMSO dimethyl sulfoxide, EO essential oil, FRAP ferric reducing activity power, FTC ferric thiocyanate (method), GC-MS gas

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chromatography mass spectrometry, HPLC high performance liquid chromatography, LPS lipopolysaccharide, LOX lipoxygenase, NMR nuclear magnetic resonance, ORAC oxygen radical absorbance capacity, ROS reactive oxygen species, STZ streptozotocin, TAC total antioxidant capacity, TBARS thiobarbituric acid reactive substances, TFC total flavonoid content, TPC total phenolic content.

# 1. Taxonomy and Archeology

Anacardiaceae (Sumac or Cashew family in English, וואַ Arabic, אלחיים Hebrew) is a medium species number family, consisting of 70-83 genera and 600-860 species. [1,2] The plants of this family inhabit all continents except Antarctica, but do not grow north of latitude line 50.[3]

Humans in our region used materials of the reviewed eight trees since very ancient times. Archeological studies from Turkey indicate that Neolithic humans used *Pistacia atlantica* fruits as food.<sup>[4]</sup> Ancient Cypriotes used six *Pistacia* species as firewood more than 8000 years ago, four out of the reviewed trees, *P. atlantica*, *P. khinjuk*, *P. lentiscus* and *P. terebinthus*, along with two other species, *P. eurycarpa* and *P. vera*.<sup>[5]</sup>

In ancient Egypt, resin of *P. lentiscus* (Mastic) was one of the embalming materials, according to a research published by T.M. Nicholson ahc (see list of abbreviations after **Keywords**).<sup>[6]</sup> They extracted the embalming material with *n*-hexane, analyzed the extracts (HPLC) and identified the compounds by GC-MS and NMR spectroscopy. They base their **conclusion mainly on the presence of several triterpenoid acids, but particularly on the concentrations ratio of oleanonic acid and moronic acid (Figure 1).** 

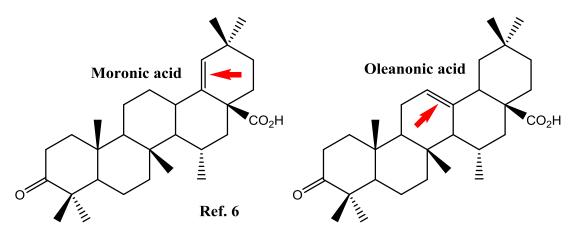


Figure 1. Oleanonic and moronic acids found in *P. lentiscus* resin used in ancient Egypt.

Ancient Egyptian culture was very colorful, and this can be clearly seen in almost all its remaining artifacts, especially textiles and texts. One of the colors that they used, ranges between very dark red and light black, was obtained by boiling aerial parts of Sumac, as reported by G. Festa ahc.<sup>[7]</sup> It is very important to notice that in the reviewed region the name Sumac refers to *Rhus coriaria*, but it may also refer to over 250 species included in this botanical genus.<sub>[8]</sub>

Finally, the Anacardiaceae trees of Israel and Palestine are *Pistacia atlantica*, *Pistacia khinjuk*, *Pistacia lentiscus*, *Pistacia palaestina* (Syn. *P. terebinthina*, *P. terebinthus*, *Lentiscus vulgaris*, *Terebinthus communis*, *T. vulgaris*), *Rhus coriaria* (Syn. *R. heterophylla*, *R. sumac*, *R. variifolia*, *Toxicodendron coriaria*), *Rhus tripartite*, *Schinus terebinthifolius*, *Searsia pentaphylla* (Syn. *Rhus pentaphylla*, *Toxicodendron pentaphyllum*).

# 2. Ethnobotany and Ethnomedicine

Trees of the Anacardiaceae family were and still being used in ethnobotany and ethnomedicine fashions in all their habitats. Firewood is still one of the major uses, along with powder of *Rhus* fruits, Sumac, as a spice. However, many other uses were documented and reported, and a summary of some of these is presented in **Table 1**.

Table 1: Selected Ethnobotanical uses of Anacardiaceae Trees of Israel and Palestine.

Species	Region*	Plant part, use objectives, reference		
	Iran	Fruits, seeds, leaves; memory enhancement, animal food, air		
		freshener, firewood, dyeing colors. <sup>[9]</sup>		
		Oil, gum, oral decoction, smoke; aphrodisiac, vaginal infections,		
		back pain, anemia. [10]		
Pistacia atlantica		Gum; wound disinfection. <sup>[12]</sup>		
Fisiacia alianiica		Seed, gum, leaves, fruits; bone and joint pains, burn healing,		
		wounds, eczema, lung infections, stomach ulcers, toothache. [13]		
	Kurdistan	Gum, fruits; stomach problems, wounds, diarrhea. [11]		
	Pakistan	Flowers, leaves, all parts; stomachache, firewood. [14]		
	Morocco	Leaves, bark; oral decoction, stomachache. [15]		
Libya		Whole plant; firewood. [38]		
Pistacia khinjuk	Iran	Gum; wound disinfection. <sup>[12]</sup>		
		Seeds, leaves; hemorrhoids, stomachache, tooth pains, memory		
		enhancement, jaundice. <sup>[13]</sup>		
		Fruits; Body reinforcement, joints and muscles pain. [16]		
	Pakistan	Flowers, leaves, all parts; stomachache, firewood. [14]		
	Turkey	Fruits, gum; inflamed wounds, gastric ulcer, aphrodisiac. [17]		
		Fruits; eaten fresh, stomachache, antiparasitic. [18]		
Pistacia lentiscus	Morocco	Leaves, bark; oral decoction, diarrhea, diabetes. [15]		
	Algeria	Leaves, fruits, oil; respiratory-, digestive-, blood-system and skin-		

		problems allergies [19,20]			
		problems, allergies. [19,20]			
		Leaves but mainly fruits oil; respiratory-, digestive-, genital-,			
		nervous-, blood-system and skin-problems. [21]			
		Leaves, fruits, aerial parts, resin; diabetes, headache, obesity,			
		cholesterol reduction, ulcer, abdominal pain, liver diseases,			
		sexual impotence, menstrual problems, mouth problems, muscle			
		pain, scars and osteoarthritis. [22]			
		Fruits, leaves; skin and gastric systems disorders. [23]			
		Leaves; decoction for digestive problems. [24]			
		Leaves, flowers; gum diseases. [25]			
	Morocco	Leaves, seeds; digestive infections, diarrhea. [26]			
		Leaves; digestive and skin problems. [27]			
		Leaves, fruits; digestive problems, ulcer, gums pain. [28]			
	Italy	Whole plant; firewood, making baskets. [29]			
	Jordan	Unspecified; medicine (unspecified). [30]			
	Palestine	Leaves; digestive and respiratory problems. [31]			
		Fruits, leaves whole plant; food, firewood, industry, colic,			
	Libya	gastritis, skin cracks, gingivitis, psoriasis, rash, colitis. [38]			
	Palestine	Leaves; joints pain, rheumatism, diabetes. [31]			
Pistacia	Tarestine	Shoots; food. [32]			
palaestina	Turkey	Fruits; hair loss and care, skin care. [33]			
	Jordan	Unspecified; food (unspecified). [30]			
	Jordan	Fruits; appetizer, spice, digestive problems. [18]			
	Turkey	Shoots; food. [32]			
		Fruits; mouth pain, diarrhea, antiparasitic, digestive problems. [33]			
D1	Inndon	Leaves, flowers; tea, spice, sour sauce. [34]			
Rhus coriaria	Jordan	Unspecified; food (unspecified). [30]			
	Palestine	Leaves, fruits; digestive and teeth problems. [31]			
		Fruits; diarrhea. [36]			
	Lebanon	Fruits, whole plant; spice, tanning of leather and textile, medicine			
		(unspecified). <sup>[35]</sup>			
	Morocco	Leaves, bark; stomachache, dyspepsia, heartburn, dysentery. [28]			
	Palestine	Leaves, fruits; digestive problems. [31]			
Rhus tripartite	Algeria	Bark, roots; gastritis. [37]			
Knus iriparitie	Libya	Leaves, fruits whole plant: food, wood industry, gastritis,			
		toothache, ulcer, eczema, skin problems, cystitis, feet			
		problems. <sup>[38]</sup>			
Schinus	Brazil	Leaves, fruits, whole plant; food, firewood, medicine			
		(unspecified). <sup>[39]</sup>			
terebinthifolius		Leaves; uterine and intestinal infections, gastritis, stomach			
		cancer. [40]			
	Morocco	Leaves; oral decoction, powder, diarrhea, diabetes. [15]			
Searsia		Leaves; stomachache, burns. [20]			
pentaphylla		Leaves; digestive and skin problems. [27]			
		Fruits; diarrhea. [28]			
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<sup>\*</sup> We preferred using "region" instead of "country" in order to avoid political controversies.

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# 3. Selected Published Activities of Rhamnaceae Trees of Israel and Palestine

These properties and activities are summarized in **Table 2**.

# Table 2: Selected Published Activities of Anacardiaceae Trees of Israel and Palestine.

# Testing Method, Results and Reference/s

# Pistacia atlantica

Fruits 80% aqueous methanolic extract was toxic to mice only in high dose of 1.66 g/kg and had antinociceptive activity tested with three tests (tail flick, hot plate, rotarod). The chemical composition was determined by GC-MS and the major components were  $\alpha$ -pinene, limonene (**Figure 4a**) and  $\beta$ -myrcene (**Figure 2**). [41]

Aerial parts aqueous extract was toxic to rats in high dose of 2 g/kg. It had analgesic (tail immersion, acetic acid-induced writhing tests) and anti-inflammatory (carrageenan-induced) activities. [42]

Galls were doubly extracted with methanol, and this extract had AChE and BuChE inhibition activities, which were affected by plant gender and harvesting time. Extract was analyzed and molecular docking was performed for two of its major active components, methyl gallate and 4,5-digalloylquinic acid (**Figure 2**). [43]

Nanoemulsion of commercial fruits EO had anti-angiogenic (chick chorioallantoic membrane assay) and anticancer (against A549 human lung cancer cells) activities. [44] Fruits 70% aqueous ethanolic extract was active against human KB cancer cells. [45]

Leaves 75% aqueous ethanolic extract was active against MCF-7 breast cancer cells. [46]

Fruits methanolic extract inhibited Ehrlich solid tumor that was induced by injection of cancer cells to mice. [47]

Leaves and stems were separately extracted with 80% aqueous methanol and both extracts were fractionized with chloroform, ethyl acetate and *n*-butanol. The six fractions were tested for AChE and BuChE inhibition, antioxidant (ABTS, CUPRAC, DPPH, FRAP methods, ethyl acetate was highest) and antiproliferative (HeLa cells) activities. The phenolic composition of the crude extract is provided. [48]

Leaves 70% aqueous ethanolic extract had antioxidant (DPPH method) and anticancer (human gastric cancer and HeLa cells) activities. TPC was determined. [49]

Resin was extracted with 0.2% aqueous polysorbate and the resulting extract had anticancer (COLO205 cancer cells) and antioxidant (ABTS, DPPH methods) activities. TPC and TFC are provided. [50]

Fruits ethanolic extract had activity against A549 human lung cancer cells. The major compounds of this extract were (%): limonene 10.92 (**Figure 4a**),  $\beta$ -pinene 4.98,  $\beta$ -myrcene 6.92, terpinolene 10.89,  $\alpha$ -terpineol 13.28, caryophyllene oxide 4.01, ethyl pentadecanoate 6.15, sapthulenol 13.45 and isosapthulenol 14.63 (**Figure 2**). [51]

Leaves aqueous extract was active against RD and Hep2 human tumor cell lines. Qualitative general and partial phenolic compositions are presented. [52]

Gel that contained 10-20% fruits EO (*n*-hexane extract) and pure EO, had ameliorative effect on acetic acid-induced colitis in rats.<sup>[53]</sup>

Resin was extracted with 0.2% aqueous polysorbate and the resulting extract had alleviating effect against acetic acid-induced colitis in rats. [54]

Resin nanoparticles had positive effect against acetic acid-induced colitis in rats. [55]

Capsules containing fruits powder had blood glucose and cholesterol lowering effect in diabetic and hyperlipidemic patients.<sup>[56]</sup>

Gum aqueous solution had glucose lowering effect in diabetic patients.<sup>[57]</sup>

Leaves methanolic extract was prepared and fractionized with *n*-hexane, chloroform, ethyl

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acetate and *n*-butanol. Crude extract was analyzed resulting mainly known phenolics. Fractions were tested for antioxidant (DPPH, FRAP and Fe<sup>+2</sup> chelating methods) and antidiabetic (inhibition of α-amylase, α-glucosidase, pancreatic lipase, pancreatic cholesterol esterase) activities, showing significant results in both tests. [58]

Leaves EO (hydrodistillation) had antioxidant (FRAP method) and antidiabetic (STZinduced in rats) activities. Antidiabetic and antihyperlipidemic activities were measured by several biomarkers including blood glucose and cholesterol concentrations. [59]

Leaves 70% aqueous methanolic extract was prepared and analyzed for general chemical composition. It was tested for anti-inflammatory (carrageenan-induced paw edema in mice), antimicrobial (against S. aureus, L. monocytogenes, B. subtilis, E. coli, P. aeruginosa, K. pneumoniae, C. albicans), antioxidant (DPPH, FRAP methods) and tyrosinase inhibition activities. [60]

Leaves 80% aqueous methanolic extract was prepared and analyzed resulting known phenolic compounds. It was tested for anti-inflammatory (carrageenan-induced paw edema in mice) and antioxidant (ABTS, DPPH, FRAP methods) activities. [61]

Seeds aqueous extract was dissolved in acetone or methanol and tested against L. ivanovii, L. innocua, L. monocytogenes, E. coli and P. aeruginosa, showing significant activity. Two other plants were studied in this research. [62]

Resin EO was prepared by hydro-alcoholic distillation, and it was active against E. coli, S. aureus and S. pyogenes. [63]

Fruits aqueous extract was active against *E.coli*, *P. aeruginosa* and *S. aureus*. [64]

Fruits and leaves were separately extracted with ethanol, and olive tree leaves were extracted as well. The three extracts were tested separately and combinedly against seven fungi species. The combination of the three extracts was most active. [65]

Leaves aqueous extract and fruits EO (hydrodistillation) were tested against six bacterial strains. EO was more active. [66]

Fruits, galls and leaves methanolic extracts were active against S. aureus, B. cereus, E. faecalis, P. aeruginosa, and E. coli. [67]

Gum EO (hydrodistillation) was active against Trametes versicolor fungus. [68]

Fruits aqueous ethanolic (ratio is not provided) extract was active against S. aureus that causes septic arthritis. [69]

Fruits powder and its aqueous extract were active against Aspergillus flavus and Aspergillus niger.<sup>[70]</sup>

Resin 70% aqueous ethanolic extract and its solution in DMSO (separately) were active against Enterococcus fecalis. [71]

Gum was analyzed for chemical composition and its major components were mentioned earlier. It had antioxidant (DPPH method) and antibacterial (six species) activities, and it extended the life of probiotics (Saccharomyces boulardii and Lactobacillus acidophilus) after encapsulation with sodium alginate in Kefir (milk drink).<sup>[72]</sup>

Leaves were successively extracted with n-hexane, ethyl acetate and methanol. The three extracts were tested against four bacteria species and one fungus, as well as antioxidant activity (DPPH method) with ascorbic acid as a reference. Chemical composition analysis revealed 2,3-Di-*O*-galloyl-D-glucose and 1,3-Di-*O*-galloyl-β-D-glucose. [73]

Fruits EO (hydrodistillation) had antioxidant (ABTS, DPPH methods) and antibacterial (E. coli, S. entritidis, S. aureus, L. monocytogenes) activities. Analysis of this EO resulted α-pinene and β-myrcene as major components. [74]

Leaves EO (hydrodistillation) had antioxidant (DPPH, FRAP methods) and antibacterial (six strains) activities. Analysis of this EO resulted terpinen-4-ol (Figure 2) as major component.[75]

Gum EO (steam distillation) was active against S. aureus, E. Coli, S. enterica, and L.

monocytogenes. Major compounds of this EO were (%): verbenone 26.19 and isobornyl acetate 29.53 (**Figure 2**).<sup>[76]</sup>

Seeds were separately extracted with water, 96% aqueous ethanol and 80% aqueous methanol. Extracts were tested for antioxidant (DPPH method) and antibacterial (15 species). In the second test extracts were active against most bacteria but were inactive against E. coli and E. aerogenes. Analysis of 80% aqueous methanolic extract revealed that germacyclopetene<sup>a</sup> is the major component, 38.12%. [77]

Leaves 90% aqueous ethanolic extract was tested for antioxidant (DPPH method) and antibacterial (six species) activities, showing significant results.<sup>[78]</sup>

Resin EO (hydrodistillation) had antioxidant (DPPH method), α-glucosidase inhibition and antimicrobial (seven bacterial and two fungal species) activities. Analysis of this EO resulted  $\alpha$ -pinene as major compound. [79]

Bark, fruits and leaves were separately extracted with 70% aqueous ethanol, and the three extracts were tested for antioxidant activity with ABTS and DPPH methods. [80]

Bark from external and internal parts of the trunk, buds, fruits, leaves, roots and stem, were separately extracted with methanol, ethyl acetate and *n*-butanol (total of 21 extracts). These extracts were analyzed for TFC and TPC, and tested for antioxidant activity by DPPH, FRAP and β-carotene bleaching methods. [81]

Hulls EO (hydrodistillation) was tested for antioxidant activity with DPPH method and analyzed for chemical composition revealing α-pinene as major component. Extraction with 50% aqueous methanol and analysis afforded known phenolic compounds: ferulic acid, quercetin, naringenin and catechin. [82]

Seeds and their epicarp were extracted with methanol and extract was analyzed for phenolics resulting known compounds. TFC, TPC, TAC and nutritional composition were determined.<sup>[83]</sup>

Galls were doubly extracted with methanol and the extract antioxidant activity was tested with ABTS, DPPH and FRAP methods. Extract analysis yielded known phenolics.<sup>[84]</sup>

Fruits aqueous extract supplementation and exercise in rats improved antioxidant biomarkers superoxide dismutase and malondialdehyde. [85]

Fruits EO (hydrodistillation) addition to sunflower oil increased its stability by improving its antioxidant capacity. t-Butyl hydroquinone (TBHQ) was antioxidant reference in this research.[86]

Fruits EO was obtained by n-hexane extraction and it was used for preparation of wound healing gel (5%). Positive effect was confirmed in cuts that were done in rats, by healing time decrease and improvement of oxidant/antioxidant parameters.<sup>[87]</sup>

Mice were cut and wounds were infected with Leishmania major. Treatment with resin compared with standard drug of glucantime showed clear positive effect. [88]

Dry fruits, leaves and fresh fruits were combinedly extracted with 80% aqueous methanol, and this extract had antiparasitic effect in lamb livers with hydatid cysts. [89]

Fruits methanolic extract had protoscolicidal effect in mice. It was toxic for healthy animals in 2.43 g/kg. Major components of this extract were (%):  $\beta$ -myrcene 41.4,  $\alpha$ pinene 32.5 and limonene 4.7.<sup>[90]</sup>

Seeds EO (ready) combined with canola oil and physical exercise ameliorated oxidative stress in patients with metabolic syndrome. The effect was measured by several oxidant/antioxidant biomarkers such as blood glucose, total antioxidant capacity, total antioxidant status, malondialdehyde and five enzymes. [91]

Gum 70% aqueous methanolic extract combined with pomegranate peel 80% aqueous methanolic extract, had antiulcer (ethanol-induced) in rats. Omeprazole was reference drug in this research.<sup>[92]</sup>

Fruits 70% aqueous ethanolic extract had anxiolytic effect in intact and gonadectomized

rats that were exposed to five different stressors. [93]

Kernels oil was prepared by cold press and it had antihyperglycemic, antihyperlipidemic and anti-inflammatory activities in fructose-fed rats. [94]

Resin EO (steam distillation) analysis showed that α-pinene is the major component. [95]

EOs of resin, fruits and leaves were separately obtained by hydrodistillation. Analysis of these EOs showed that the major components were  $\alpha$ -pinene in resin, bornyl acetate in fruits and terpinen-4-ol in leaves. [96]

Fruits (Algeria) were separately extracted with diethyl ether and chloroform-methanol 2:1 v/v. Both extracts were analyzed for nutritional components, fatty acids and lipids, mainly plant sterols. Results were compared with analysis of *Pistacia vera* (Turkey). [97]

Follow up of previous study but in this research the chemical composition of resin EO was compared with EOs from other regions and other species: P. atlantica from Iran and Morocco, P. eurycarpa from Turkey and P. lentiscus from Turkey, Greece and Morocco. In all cases,  $\alpha$ -pinene is the major component. [98]

Leaves EO (hydrodistillation) analysis afforded  $\alpha$ -pinene as major component. [99]

Seeds oil was prepared by cold press and was analyzed for fatty acids and lipids, resulting 14 acids and 7 phytosterols, where  $\beta$ -sitosterol (**Figure 2**) was 87.73%. [100]

Fruits oil was prepared by n-hexane extraction and it was analyzed for chemical composition. Fatty acids composition is also presented. [101]

Resin was analyzed for detailed nutritional, mono and polysaccharide and amino acids compositions. Its 90% aqueous ethanolic extract was analyzed for chemical composition and some thermal properties of the resin (for example, decomposition temperature range) were also studied. [102]

Fruits from four locations EOs were prepared by n-hexane extraction, their nutritional composition was analyzed and their TPC was determined by 80% aqueous ethanolic extract. The phenolic composition was analyzed by 80% aqueous ethanolic extract. [103]

Gum aqueous extract had cyto-genotoxicity against NIH-3T3, KB and HUVEC cell lines. Tests confirmed cells DNA fragmentation. [104]

Capsules containing 350 mg of resin and 150 mg of sugar were supplemented to patients with functional dyspepsia, resulting notable ameliorating effect. [105]

Fruits aqueous extract was orally supplemented to rats resulting hepatoprotective effect, measured by several biomarkers such as glutathione peroxidase, total oxidative capacity, cholesterol and triglycerides. [106]

Leaves 70% aqueous ethanolic extract had hepatoprotective effect in  $CCl_4$ -induced toxicity in rats, measured mainly by functioning of liver enzymes. [107]

Fruits oil obtained by cold press was used to treat rats with levothyroxine-induced (12 mg/L) hyperthyroidism. Positive effect was measured by serum leptin concentration. [108]

A follow up study: same oil in the previous research was used to treat propyl thiouracil-induced hypothyroidism. Same biomarkers were measured for effect observation. [109]

Fruits methanolic extract did not alleviate Cd(II) kidney toxicity in rats but improved antioxidant biomarkers such as lipid peroxidation. [110]

Mice with liver and kidney injury induced by busulfan were supplemented with diet that included 10% (plant part is not mentioned), resulting improvement of histological parameters, especially liver and kidney enzymes.<sup>[111]</sup>

Resin EO (hydrodistillation) was used to prepare a cream for treatment of patients with knee osteoarthritis. Compared with standard drug of diclofenac, results showed clear positive effect. Chemical compositions of EO and cream were analyzed resulting  $\alpha$ -pinene as major component. [112]

Gum was used to prepare an ointment for treating old patients with knee osteoarthritis, resulting clear improvement expressed by patients and some biomarkers.<sup>[113]</sup>

Gum was used to prepare an ointment for treating patients with knee osteoarthritis, resulting clear improvement. α-Pinene was the major component of this ointment, and the reference drug was acetaminophen.[114]

Gum and its EO (hydrodistillation) were supplemented to ovariectomy-induced osteoporotic rats, directly or in their encapsulated form. Positive results were recorded in physical (three-point bending) and biochemical (serum calcium) tests. α-Pinene was the major component of this EO. [115]

Peeled seeds were extracted with 0.5 M NaCl (aq) solution, and the resulting extract was used to remove arsenic (Na<sub>2</sub>AsO<sub>4</sub>) from its aqueous solution. [116]

Same extract as in previous research was used by the same group for removal of organic pollutants. [117,118]

Resin EO (hydrodistillation) gel had healing activity of burn wounds of rats skin along with angiogenesis activity. α-Pinene was the major component of this EO.<sup>[119]</sup>

Resin 95% aqueous ethanolic extract was used to prepare an ointment that had healing activity of burn wounds of rabbits skin. Activity was physically observed and tested by biochemical parameters, mainly oxidant/antioxidant. [120]

Resin EO (hydrodistillation) ointment had healing activity of burn wounds of rats skin. physically observed and tested by biochemical was oxidant/antioxidant, vasculoendothelial growth factor and hydroxyproline. [121,122]

Fruits 50% aqueous ethanolic extract had activity against five bacterial and three fungal species.[123]

Fruits EO was obtained by n-hexane extraction and had significant antioxidant activity, measured by DPPH and β-carotene bleaching methods. EO was analyzed for TFC, TPC and fatty acids composition resulting detection of nine compounds. [124]

Fruits EO (hydrodistillation) and 50% aqueous ethanolic extract were prepared. Major component of EO was α-pinene (93.2%). TFC, TPC and antioxidant (DPPH, TAC methods) activity of extract were determined. [125]

Dehulled seeds had beneficial effect when used as part of poultry diet. [126]

Leaves ethanolic extract was fractionized with ethyl acetate and n-butanol. The crude extract was active against eight bacterial and six fungi species. Its antioxidant activity was tested by FRAP and superoxide radical scavenging methods. Extract and fractions were analyzed for chemical compositions resulting mainly known phenolic compounds. [127]

Leaves and resin were separately extracted with 80% aqueous ethanol. Extracts were analyzed for TFC and TPC, and their antioxidant activities were determined with DPPH and FRAP methods. Their antifungal activities were tested against P. digitatum. [128]

a- to the best of our search efforts, germacyclopetene does not exist.

# Pistacia khiniuk

Fruits 50% aqueous ethanolic extract had activity against five bacterial and three fungal species.[123]

Fruits EO was obtained by *n*-hexane extraction and had significant antioxidant activity, measured by DPPH and β-carotene bleaching methods. EO was analyzed for TFC, TPC and fatty acids composition resulting detection of ten compounds. [124]

Fruits EO (hydrodistillation) and 50% aqueous ethanolic extract were prepared. Major component of EO was α-pinene (78.71%). TFC, TPC and antioxidant (DPPH, TAC methods) activity of extract were determined. [125]

Dehulled seeds had beneficial effect when used as part of poultry diet. [126]

Leaves, roots, stems and germinated branches from seeds; were all extracted with ethanol, but only the last extract was tested for biological activities. It inhibited several enzymes (not AChE), was cytotoxic (against MCF-7 and HT-29 cancer cell lines) and had hypotensive activity measured by inhibition of angiotensin I-converting enzyme (ACE).[129]

Dehulled fruits 70% aqueous ethanolic extract was administered (200 or 400 mg/kg) to rats, resulting reduction of blood glucose and lipids.  $^{[130]}$ 

Leaves 95% aqueous ethanolic extract had blood lipid lowering activity in high fat-fed rats, with standard drug of simvastatin as a reference. [131]

Leaves 95% aqueous ethanolic extract was tested for anti-inflammatory activity in rats (carrageenan-induced paw or ear edema) by testing several biomarkers. Extract was analyzed for chemical composition where seven major phenolics were detected, including three digalloyl-D-glucose derivatives <sup>a</sup> (**Figure 3**). [132]

Leaves EO (hydrodistillation) and chloroform, ethyl acetate, diethyl ether and ethanolic extracts were separately prepared. The four extracts were tested against six bacteria and two fungi species showing moderate to high activities. EO was analyzed for chemical composition resulting spathulenol as major component. [133]

Fresh leaves EO (hydrodistillation) was active against *C. albicans*, and  $\gamma$ -terpinene (**Figure 3**) was its major component. [134]

Fruits EO (cold press) and methanolic extract were separately prepared and tested against *S. aureus*, *E. coli* and *P. aeruginosa*. Fatty acid compositions were determined. [135]

Gum EO was obtained by conventional microwave-assisted hydrodistillation, and both were tested against eight bacteria species. Major component of these EOs was  $\alpha$ -pinene. [136]

*In vivo* grown stocks ethanolic extract had antioxidant (ABTS, DPPH, CUPRAC methods) and antibacterial (against four bacteria and a fungal species) activities. [137]

Aerial parts EO (hydrodistillation) was active against *E. coli* and *S. aureus*, and  $\gamma$ -terpinene was its major component. [138]

Leaves EO (hydrodistillation) was active against *P. aeruginosa* and *B. subtilis*, and  $\gamma$ -terpinene was its major component. [139]

Hull EO (hydrodistillation) had anticancer (MCF-7 human cancer cells), antibacterial (against six species) and antioxidant (DPPH and  $\beta$ -carotene bleaching methods) activities. The major component of this EO was  $\beta$ -caryophyllene, 25.32%. [140]

Fruits were separately extracted with n-hexane, ethyl acetate, ethanol and methanol, and the general chemical compositions of the four extracts were determined. Extracts were tested for antioxidant (DPPH method) and antibacterial (against four species) activities. [141]

Gum EO (ultrasound-assisted hydrodistillation) was used to prepare a nanoemulsion that was active against ten bacterial strains.  $\gamma$ -Terpinene was the EO major component. [142]

Gum nanoparticles had activity against *P. aeruginosa* and *S. aureus* and  $\beta$ -TC3 cells. In both cases, the activities of the nanoparticles were higher than those of gum. [143]

Hull and kernels EOs were separately prepared by n-hexane extraction and were tested for antioxidant activity using peroxide value method. Chemical compositions were analyzed for fatty acids (seven in hull EO and eight in kernel EO) and tocopherol/tocotrienol (six in both, **Figure 3**). [144]

Fruits different parts were extracted with methanol and antioxidant activity (DPPH, FRAP, NO scavenging methods), TFC and TPC were determined. [145]

Fruits 60% aqueous ethanolic extract was used to prepare a nanoemulsion which extended shelf life of sunflower oil. The antioxidant (DPPH, FRAP methods) activity of this extract was determined. [146]

Aerial parts methanolic extract antioxidant activity was determined by TAC and FRAP methods. [147]

Fruits methanolic extract was fractionized with *n*-hexane, chloroform, ethyl acetate and *n*-butanol. TFC, TPC and antioxidant (TAC, lipid peroxidation inhibition methods) were

determined.[148]

Leaves 70% aqueous ethanolic extract had ameliorative effect of alkali-induced eye injury in rabbits. Effect was physically detected and by measurement of glutathione peroxidase and reduced glutathione concentrations. [149]

Fruits 70% aqueous ethanolic extract had antiparasitic activity against *Leishmania tropica* and *Leishmania major* in infected mice (*in vivo*) and against promastigotes (*in vitro*). Extract had cytotoxic activity against J774-A1 cells. [150]

Fruits 80% aqueous methanolic extract had activity against hydatid cysts protoscoleces. The toxicity of this extract was 2.8 g/kg in mice. [151]

Fruits major component was α-pinene. [152]

Fruits EO (*n*-hexane extraction) contained ten fatty acids. [153]

Growth under NaCl stress increased the production of the following triterpenoid acids in leaves, roots and shoots: ursonic, moronic, oleanonic, masticadienolic (**Figure 3**), oleanolic and ursolic.<sup>[154]</sup>

Seeds aqueous and methanolic extracts had cytotoxic activity against Rhabdomyosarcoma, AMN-3 and L20B cell lines. They also increased human blood lymphocyte proliferation (mitogenic activity). [155]

Leaves EO had insecticidal activity against *Agonoscena pistaciae*. The major components of this EO were (%): β-myrcene 18.7 (**Figure 2**), α-eudesmol 12.3, β-eudesmol 9.3, 1,7-di-epi-β-cedrene 7.3, bicyclogermacrene 5.6 and  $\gamma$ -eudesmol 4.9 (**Figure 3**). [156]

Leaves methanolic extract had insecticidal activity against *Tribolium confusum* and *Oryzaephilus surinamensis*. The major components of this extract were (%): 5-ethoxy-4-phenyl-2-isopropylphenol 29.02, phenyl ethyl alcohol 10.78, benzyl alcohol 7.8 and 1,2-benzenediol 6.67. [157]

Resin methanolic extract was cytotoxic to HUVEC and Y79 cells and had antiangiogenic effects against endothelial cells.  $\alpha$ -Pinene was the major component of this extract. In this research, *P. vera* was also studied. [158]

Aerial parts ethanolic extract healing effect on skin incision of Achilles tendon in rabbits. Effect was physically observed and measured by oxidant/antioxidant biomarkers. [159]

a- In the names of two of these compounds it is indicated that the glucose epimer is  $\beta$  while the drawn structure is  $\alpha$ .

b- Mistakenly written "δ-eudesmol".

#### Pistacia lentiscus

Leaves methanolic extract had high antioxidant activity measured by DPPH method. General chemical composition is presented. [22]

Leaves and stem 80% aqueous ethanolic extract had notable antioxidant activity tested by DPPH and  $\beta$ -carotene bleaching method. Leaves EO (hydrodistillation) was analyzed and the major components are shown in **Figure 4a**. [23]

Leaves ethanolic extract was fractionized with ethyl acetate and *n*-butanol. The crude extract was active against eight bacterial and six fungi species. Its antioxidant activity was tested by FRAP and superoxide radical scavenging methods. Extract and fractions were analyzed for chemical compositions resulting mainly known phenolic compounds. [127]

Leaves were extracted with 80% aqueous ethanol and extract was analyzed for TFC and TPC, and its antioxidant activity was determined with DPPH and FRAP methods. Its antifungal activity was tested against *P. digitatum*. <sup>[128]</sup>

Resin 60% aqueous methanolic extract had intracellular antioxidant glutathione (GSH) restoration activity in peripheral blood mononuclear cells that were exposed to oxidized low-density lipoprotein, that has atherogenic effect. [160]

Fruits and leaves EOs were separately prepared by hydrodistillation. Both EOs had anticancer (against RD and L20b cancer cells), antioxidant (ABTS, DPPH, FRAP

methods), antibacterial (against eight bacterial strains) and antiparasitic (against *Leishmania infantum*, *L. major*, *L. tropica*) activities. Major components of these EOs were (%): leaves,  $\beta$ -myrcene 33.46 and  $\alpha$ -pinene 19.20; fruits, limonene 18.26 and  $\alpha$ -pinene 20.46. [161]

Commercial aerial parts EO was analyzed and its major components were (%):  $\beta$ -myrcene 25.25 and  $\alpha$ -pinene 18.64. It had anticancer (against CaCo-2, FTC-133, HeLa, HepG2, LNCaP, MDA-MB-231 and NCI-H1975 cell lines. AG-09429 were as control cells). Effect was measured by cell apoptosis and scavenging activity of ROS. [162]

Resin EO (hydrodistillation) contained  $\alpha$ -pinene and  $\beta$ -myrcene as major ingredients. EO was more active against HT29 and Caco-2 cancer cells (*in vitro*) and against colon cancer (*in vivo*) in mice (oral administration). [163]

Gum supplementation to patients with diabetic gastroparesis resulted clear ameliorating effect, with levosulpiride as standard drug in the control group. [164]

Leaves 80% aqueous acetonic extract was analyzed for TFC, TPC and phenolic compounds, resulting catechin, gallic acid and quercetin 3-glucoside as major components. Extract had significant antioxidant activity measured with DPPH and  $\beta$ -carotene bleaching methods. A moderate  $\alpha$ -amylase inhibition activity was recorded, compared with acarbose, gallic acid, catechin and quercetin. [165]

Fruits EO was analyzed for chemical composition resulting  $\alpha$ -pinene and limonene as major components. Extract and both compounds had antioxidant (ABTS, DPPH, FRAP methos, with Trolox and ascorbic acid as references), antidiabetic ( $\alpha$ -amylase and  $\alpha$ -glucosidase inhibition with acarbose as a reference) and dermatoprotective (tyrosinase and elastase inhibition with quercetin as a reference) activities. [166]

Mature fruits EO was prepared by cold press, and it was analyzed for TFC, TPC and unsaponifiable (KOH/ethanol) fraction. Extract and fraction had antidiabetic ( $\alpha$ -amylase and  $\alpha$ -glucosidase inhibition with acarbose as a reference), neuroprotective (AChE and BuChE inhibition, with galantamine as a reference) and antioxidant (DPPH, CUPRAC methods, with BHA, BHT as references) activities. [167]

Fruits EO was prepared by cold press and it had antihyperlipidemic (egg yolk-fed *Oryctolagus cuniculus* rabbits) activity, measured by body weight and blood lipid biomarkers. [168]a

Resin dissolved in sesame oil had alleviating effect on acetic acid-induced colitis in rats. Effect was measured by several biomarkers, especially myeloperoxidase. Prednisolone was reference drug in this study. [169]

EO of young leaves and stems (hydrodistillation) was used to prepare a hydrosol, which was active against LPS- induced inflammation in human monocytes and U937 cells. [170]

Leaves were separately extracted with n-hexane, ethyl acetate, ethanol and water. These extracts were analyzed for TFC and TPC, and tested for antioxidant activity (DPPH, FRAP methods, ethanolic extract most active, BHA and ascorbic acid references) and anti-inflammatory activity (albumin denaturation method, voltarene reference, ethanolic extract most active). [171]

Fruits were extracted with a mixture of eleven solvents, including p-cymene,  $\alpha$ -pinene, limonene; that are ingredients of the of the resulting oil. The resulting oil had high anti-inflammatory activity measured by inhibition of NO production in RAW 264.7 microphages. [172]

Leaves 80% aqueous methanolic extract was prepared and analyzed for TFC and TPC. It had anti-inflammatory activity tested with three methods: croton oil-induced ear edema in mice, acetic acid-induced vascular permeability in mice and carrageenan-induced pleurisy in rats. Extract immunomodulatory effect was tested in human neutrophils. [173]

Gum EO (hydrodistillation) was active against P. fragi, S. enteritidis, S. aureus and L.

plantarum.[174]

Leaves EO (hydrodistillation) and aqueous extract were active against nine bacteria and three fungi species: moderate against bacteria and weak against fungi. [175]

Fruits EO (cold press) was active against four *Streptococcus* species. [176]

EO was obtained by heating fresh fruits paste, and it was tested against six bacteria and four fungi species. [177]

Fruits and leaves were separately extracted with water and ethanol, and the four extracts had high activity against *E. coli*, *S. aureus* and *K. pneumoniae*. [178]b

Resin 96% aqueous ethanolic extract had activity against S. aureus and E. coli. [179]

Several formulation that contained gum and amoxicillin (standard antibiotic) were tested for swelling index and kinetics of active components release. [180]

Leaves and stems were extracted with 80% aqueous ethanol, and extract was fractionized with petroleum ether, chloroform, ethyl acetate, *n*-butanol and water. Extract and fractions had antimicrobial (four bacteria and two fungi species) and antioxidant (DPPH method) activities. General chemical composition was determined for each material. [181]

Leaves, resin and twigs EOs (steam distillation) were active against six bacteria and three fungi species. EOs were analyzed for chemical compositions, and the major components were  $\beta$ -myrcene and germacrene D (leaves, twigs),  $\alpha$ -pinene and  $\beta$ -myrcene (resin). [182]

Gum EO was obtained by reduced pressure distillation starting from 20 °C and reaching 140 °C, obtaining four more fractions. Gum, EO, fractions and twelve of major gum components were tested for antibacterial activity against *E. coli*, *S. aureus* and *B. subtilis*. Chemical composition of gum, EO and fractions was analyzed and the results were (%): gum,  $\alpha$ -pinene 40.9, *Z*,*Z*-farnesol 11.9 (**Figure 4a**); EO,  $\alpha$ -pinene 63.3,  $\beta$ -myrcene 25.0; fraction1,  $\alpha$ -pinene 66.3,  $\beta$ -myrcene 13.1; fraction2,  $\alpha$ -pinene 52.6,  $\beta$ -myrcene 21.6; fraction3, *trans*-verbenol 9.6 (**Figure 4a**),  $\beta$ -myrcene 7.8; fraction4,  $\beta$ -myrcene 17.0, *trans*-verbenol 10.4. [183]

Leaves EO (hydrodistillation) was active against *K. pneumonia* and *P. aeruginosa*, and its major components (**Figure 4a**) were (%): germanicol 12.8, thunbergol 8.8. [184]

Commercial gum EO had activity against eight bacteria and two fungi species. The major components of this EO were  $\alpha$ -pinene and  $\beta$ -myrcene. [185]

Commercial gum was analyzed to obtain 24*Z*-isomasticadienolic acid, oleanolic acid and oleanonic aldehyde (**Figure 4a**). These compounds were active against eleven bacterial species.<sup>[186]</sup>

Fresh ripe fruits EO (hydrodistillation) was active against three bacteria and two fungi species. The major components of this EO were (%):  $\alpha$ -terpineol 23.78 and 2-undecanone 11.72. [187]

Gum EO (hydrodistillation) was active against five fungal and three bacterial species. Analysis of EOs from differently aged gums resulted different chemical compositions, but in average, major components were  $\alpha$ -pinene and  $\beta$ -myrcene. [188]

Aerial parts EO (hydrodistillation) was active against *E. faecium*, *B. subtilis*, *S. aureus*, *E. coli*, *Y. enterocolitica* and *P. aeruginosa*. Major components (**Figure 4a**) of this EO were (%): linalool formate 28.86 and  $\alpha$ -longipinene 16.13. [189]

Encapsulated resin EO (hydrodistillation) was active against *S. aureus*, *E. coli* and *P. aeruginosa*. Major components of this EO were  $\alpha$ -pinene and  $\beta$ -myrcene. [190]

Leaves 85% aqueous methanolic extract was analyzed for TFC and TPC. It was fractionated with n-hexane, chloroform and ethyl acetate. The extract and fractions were tested for antioxidant activity with DPPH, hydroxyl scavenging, FRAP,  $\beta$ -carotene bleaching and FTC methods. BHT was reference in these tests. [191]

Aerial parts were separately extracted with diethyl ether, dichloromethane, ethyl acetate, methanol and water. Extracts were analyzed for phenolics families and tested for

antioxidant activity with DPPH and FRAP methods. [192]

EO was obtained from fruits powder with hot water extraction and had anti-bleomycin-induced lung fibrosis in rats. Activity was measured by physical parameters (body weight) and oxidant/antioxidant biomarkers (superoxide dismutase and catalase). The major components of this EO were (%): linoleic 70.6 and palmitic 24.7, acids. [193]

Shoots were separately extracted with ethyl acetate and water and the general compositions of extract were determined. The presence of cortisone (**Figure 4a**) is reported. [194]

Leaves EO was obtained by extraction with petroleum ether, and separately, methanolic extracts of fruits and leaves were prepared. EO and extracts were analyzed for TFC, TPC, anthocyanins, and were tested for antioxidant activity with DPPH, hydroxyl radical scavenging and FRAP methods. Procyanidin A2 (dimer) (**Figure 4b**) was detected in aqueous extract. [195]

Leaves from four locations (Morocco) were extracted with 80% aqueous methanol and TFC, TPC, condensed tannins and ascorbic acid contents were determined. Antioxidant activity of the extracts was determined with DPPH and TAC methods. [196]

Leaves ethanolic extract enhanced milk constituents in bovine mammary epithelial cells by modulation of their oxidative status.<sup>[197]</sup>

Gum and leaves were separately extracted with acetone, ethanol and methanol (6 extracts). Extracts cytotoxic activity was tested against CCD-34 LU, HEK293, HeLa, HepG2, MDA-MB-231, PANC-1, PC-3, A549, RAW 264.7 cell lines; and their antiviral activity was tested against bronchitis virus strain D274. The phenolic and fatty acid compositions of extracts were determined. [198]c

Aerial parts from three different locations (Morocco) were harvested at seven consecutive month (December-June) and their EOs (hydrodistillation) were prepared. All 21 EOs were analyzed revealing significant differences in their chemical compositions, but the major components were as shown in **Figure 4a**, by N. Souilah ahc (Ref. 23). [199]

Leaves EO (hydrodistillation) analysis resulted close results to those of previous study, from one location.  $^{[200]}$ 

Leaves EO (hydrodistillation) from two locations in Spain. Results are close to N. Souilah ahc (Ref. 23). Interesting table of comparison between many EOs compositions from different countries is presented. [201]

Seeds EO (n-hexane extraction) from high locations in Morocco. Fatty acids composition is presented. [202]

After heat extraction of leaves EO, the remaining powder was used as biosorbent for removal of rhodamine B and ethyl violet from their aqueous solutions. Kinetics of decolorization is reported. [203]

Leaves methanolic extract was fractionized with ethyl acetate and water, their TFC and TPC were determined. The antioxidant activity of the three materials was tested with DPPH and FRAP methods, with ascorbic acid as reference. Ethyl acetate fraction was used to prepare a dermatoprotective cream (5%, transdermal diffusion test). Same extract and its major components were tested for tyrosinase, elastase and B16 cells inhibition. Twenty-six known phenolics were isolated from ethyl acetate extract along with other compounds like lupeol and loliolide (**Figure 4b**). [204]

Leaves were extracted with supercritical- $CO_2$  and EO had ameliorative effect in carotid arteries in rats. The major components of this EO were (%):  $\alpha$ -pinene 6.3, germacrene D 19.9,  $\beta$ -caryophyllene 6.6 (**Figure 4a**),  $\gamma$ -cadinene 8.7, sabinene 5.8 (**Figure 4b**). [205]

Fresh fruits paste was mixed with cold water and the floated oil was mechanically decanted. This EO was supplemented to mice for five days and testing the physical situation of the animals, as well as ten biomarkers, indicated that this EO is safe. Authors

suggest that treatments that include this EO in combination with other drugs should be examined carefully. [206]

Comprehensive analysis of leaves to the level of trace elements showed that use of these leaves for medicinal plants in traditional style is safe. [207]

Fruits EO was isolated from paste mixture with cold water and was analyzed for fatty acids composition, resulting the presence of five free acids. EO was safe to normal human dermal fibroblasts. EO contained five fatty salicylic acid derivatives (**Figure 4b**). [208]

Fruits EO was obtained by cold press and it was used to prepare and ointment that treated mechanical skin wounds in guinea pigs. Healing was tested by physical contraction of wounds and hematoxylin and eosin staining of granulation tissue.<sup>[209]</sup>

- a- This article title includes a mistake: "Effets" (French) instead of "Effects" (English).
- b- This article includes several notable mistakes. For example, in "preparation of the extracts" section it is written "planet material" instead of "plant material". And more important, in the "test organisms" section, two out of three names are mistaken: *E. coli, S. aereus (aureus)* and *Klebsilla (Klebsiella) pneumoniae*.
- c- In table 1 in this article, "Phenolic and flavonoid content of different *P. lentiscus* leaves (mg kg-1 extract) from trees of different ages" is presented. Reading the table reveals that the compound with highest concentration is fumaric acid, which is not phenolic or flavonoid.

# Pistacia palaestina

Comprehensive analysis of leaves to the level of trace elements showed that use of these leaves for medicinal plants in traditional style is safe. [207]

Resin extract caused apoptosis of MDA-MB-231 breast cancer cells with a dose of (IC<sub>50</sub>) of 56.54  $\mu g/mL$ . [210]

Seeds EO (hydrodistillation) was active against human leukemic K562 cells. [211]

Fruits EO (hydrodistillation) had activity against HCT116 cancer cells. The major components of this EO were (%):sabinene 29.8,  $\alpha$ -pinene 19.8,  $\beta$ -pinene 13.1,  $\alpha$ -terpineol 10.3. [212]

Fresh unripe fruits EO (hydrodistillation) was active against A549 cell lines. The major components of this EO were stearic acid (n-C<sub>17</sub>H<sub>35</sub>CO<sub>2</sub>H) 21.86% and isopropyl palmitate (n-C<sub>15</sub>H<sub>31</sub>CO<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>) 13.47%. [213]

Galls were successively extracted with methanol, dichloromethane and ethyl acetate. These extracts were analyzed for chemical compositions affording three compounds: masticadienolic acid (**Figure 3**, ref. 154), masticadienonic acid and morolic acid, (**Figure 5**). These compounds had anti-inflammatory activity, where inflammation was induced in rats with for methods. [214]

Leaves were separately extracted with ethyl acetate, methanol and water, and the extracts had weak activity against six bacteria and two fungi species. [215]

Methanolic extract of leaves, seeds and stems were used to prepare chitosan films for active packaging. These films had antioxidant (DPPH method), antibacterial (nine species) and anti-quorum sensing (*Chromobacterium violaceum*) activities. Extracts were analyzed for phenolics resulting 12 in leaves extract, 8 in seeds extract and 7 in stem extract. [216]

EOs (hydrodistillation) of ripe and unripe fruits, and methanolic extracts were prepared. The four materials were analyzed for ascorbic acid content, TFC, TPC and tested for  $\alpha$ -glucosidase inhibition activity. Antioxidant activity was tested with ABTS, DPPH, FRAP and TAC methods; and antibacterial activity was tested against 13 bacteria species. Major phenolic components of these fruits methanolic extracts were syringic acid and rutin; while major components of EOs were  $\alpha$ -pinene and  $\alpha$ -terpinolene (unripe) and  $\alpha$ -pinene,  $\alpha$ -terpinolene and cis- $\beta$ -ocimene (**Figure 5**) (ripe).

EOs (hydrodistillation) of fruits, fruit pedicels, galls and leaves were prepared from plants in three different locations in Kosovo. These EOs were tested against *S. aureus* (galls most active), with tea tree oil and two standard antibiotics as references. The major components of these EOs were (average, %): α-pinene 39.4, D-limonene 30.1, cis-β-ocimene 21.3 and β-pinene 11.6. [218]

Aerial parts aqueous extract had activity against hydrogen peroxide-induced in rats. Effect was measured with TBARS method, amount of glutathione in tissues (seven organs), glutathione peroxidase enzyme activity and superoxide dismutase. [219]

Leaves 96% aqueous ethanolic extract was analyzed for TFC and TPC, and tested for antioxidant activity with ABTS, CUPRAC, DPPH and FRAP methods. Qualitative phenolics composition is presented.<sup>[220]</sup>

Fruits methanolic extract was tested for antioxidant activity (DPPH, FRAP methods) and analyzed for TPC. [221]

Fruits EO (petroleum ether extraction) and methanolic extract of the remaining powder were prepared. Extract was analyzed for TFC, TPC and tocopherols content, and its antioxidant activity was tested with DPPH method. The analysis of the EO composition resulted eleven fatty acids and eleven phytosterols, where  $\beta$ -sitosterol had highest concentration (85.6%), followed by campesterol (4.47%, **Figure 5**). [222]

Leaves methanolic and ethyl acetate extracts were prepared, analyzed for TPC and tested for antioxidant (ABTS, CUPRAC, DPPH, FRAP methods) and for enzyme inhibition ( $\alpha$ -amylase,  $\alpha$ -glucosidase, AChE, BuChE and tyrosinase) activities. Detailed qualitative phenolic compositions are presented. [223]

Resin was tested for antioxidant activity (DPPH) and had preservative effect on wine. [224] Fresh fruits and leaves were separately extracted with 60% aqueous methanol and water (four extracts), and hydro-methanolic extract was analyzed for TFC, TPC, qualitative phenolic composition, and tested for antioxidant activity with DPPH method. It was used to prepare an ointment (5%) had healing effect of mechanical wounds in rats skin. Effect was measured by wound contraction. [225]

Fruits and leaves were extracted with 80% aqueous methanol and they were used to treat isoproterenol-induced cardiac ischemia in rats. Positive effect was measured by five tests: catalase, glutathione peroxidase, glutathione, superoxide dismutase and TBARS.<sup>[226]</sup>

EOs (hydrodistillation) were prepared from young shoots, flowers, unripe and ripe fruits, and their chemical compositions were analyzed. Notable differences were detected. For example, p-cymene was found only in young shoots (27.3%) while  $\alpha$ -cadinol was present only in flowers (2.7%), see **Figure 5**. In addition, almost all compounds concentrations varied according to plant part. For example, the concentrations of D-limonene were (%): 3.0 young shoots, 9.4 flowers, 34.2 unripe fruits and 32.8 in ripe fruits. [227]

In principle, this study is similar to the previous research, where EOs (hydrodistillation) were obtained from leaves, galls, unripe and ripe fruits. Similar notable differences were detected in components content and concentrations. For example, the concentrations (%) of  $\alpha$ -pinene were: 63.1, 49.4, 5.3 and 6.5, respectively. [228]

Fruits nutritional values were determined and EO (hydrodistillation) was analyzed for fatty acids (ten). Its physiochemical properties are also reported: relative density, refractive index, acidity, peroxide value, saponification number, unsaponifiable matter, carotenoid content and iodine value. [229]

Similar research to previous two studies with the following differences: leaves, fruits and fruitful twigs were the used plant parts, research was done using trees in Sardinia. For example, the concentrations (%) of  $\alpha$ -pinene were: 16.4, 66.0 and 54.8, respectively. [230]

Follow up to studies cited in references 227 and 229, with more details and plants harvested in fourteen/fifteen locations. [231,232]

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Seeds were separately extracted with n-hexane, n-heptane, petroleum ether and carbon tetrachloride. Nutritional values and fatty compositions of extracts were determined. [233]

Commercial EO had alleviative effect in female rats with ovarian ischemia and reperfusion injury. [234]

Seeds powder was included (10-50 g/kg) in laying hens diet resulting improvement of the quality of eggs: weight, shell breaking strength, egg protein and yolk color. [235,236]

Unroasted and/or roasted (different temperatures) fruits were included in cookies/noodles resulting improvement of their physical (sensory, color and others) and nutritional (total dietary fiber, phytic acid and others) properties. Cookies/noodles antioxidant activity was tested with DPPH method. [237,238]

Roasted fruits were used to prepare "coffee" Middle-Eastern style (boiling plant powder, stable sugar and water), and it had healing effect in thioacetamide-induced liver injury in rats. Effect was measured with several biomarkers concentrations such as transforming growth factor beta (TGF- $\beta$ ), nuclear factor kappa B (NF)- $\kappa$ B and tumor necrosis factor alpha (TNF- $\alpha$ ). [239]

Fruits isopropyl alcohol extract had ameliorative effect against DMBA-induced <sup>a</sup> liver/brain cancer in rats. Positive effect was measured by several biomarkers such as superoxide dismutase, malondialdehyde, glutathione S-transferase and lipid peroxidation (TBARS method). [240,241]

a- DMBA 7,12-dimethylbenz[a]anthracene

#### Rhus coriaria

Fruits volatiles were obtained from fruits by micro-extraction, and the major components were (%):  $\alpha$ -pinene 16.3, limonene 11.5,  $\beta$ -caryophyllene 15.4 (**Figure 4a**) and 3,7-dimethyl-1,3,6-octatriene 12.3 (**Figure 6**). [34]

Leaves were extracted with 80% aqueous ethanol and extract was analyzed for TFC and TPC, and its antioxidant activity was determined with DPPH and FRAP methods. Its antifungal activity was tested against *P. digitatum*. <sup>[128]</sup>

Resin methanolic extract was cytotoxic to HUVEC and Y79 cells and had antiangiogenic effects against endothelial cells.  $\alpha$ -Pinene was the major component of this extract. [158]

Fruits isopropyl alcohol extract had ameliorative effect against DMBA-induced liver cancer in rats. Positive effect was measured by several biomarkers such as superoxide dismutase, malondialdehyde, glutathione S-transferase and lipid peroxidation (TBARS method). [240,241]

Unripe fruits 70% acetonic and 80% methanolic extracts were prepared and tested for anti-angiogenic effect with chorioallantoic membrane assay, with thalidomide as a reference. Acetonic extract was active individually and had a very strong synergetic effect with tannic acid (**Figure 6**), a natural product found in *Rhus* genus plants. [242]

Fruits 70% aqueous ethanolic extract was active against MCF-7, PC-3 and SKOV3 cancer cell lines, with clioquinol and acetazolamide as references. Partial qualitative chemical composition of the extract is presented. [243]

Fruits aqueous and ethanolic extracts were separately tested for anticancer (against MCF-7 and HT-29 cancer cell lines with 5-fluorouracil as a standard), antidiabetic (inhibition of  $\alpha$ -amylase and  $\alpha$ -glucosidase) and anticholinergic (AChE and BuChE inhibition) activities. Phenolic compositions of both extracts are presented. [244]

Commercial fruits powder (sumac) was extracted with 70% aqueous ethanol inhibited uterus cervix cancer cells migration, and had wound healing activity, tested with HeLa cells. Partial qualitative chemical composition of the extract is presented. [245]

Fruits 80% aqueous methanolic extract was analyzed for TPC and was not used for other purpose. Fruits powder was added to broilers diet resulting decrease of blood glucose and lipids but increased abdominal fat.<sup>[246]</sup>

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Fruits powder (sumac) was supplemented to human diabetics resulting decrease of blood glucose and improvement of other biomarkers. In addition, TAC of patients blood increased from 2.45 to 3.30  $\mu mol/L.^{[247]}$ 

Sumac aqueous extract had blood glucose lowering effect in alloxan-induced diabetic rats, and increasing antioxidant activity, measured with malondialdehyde concentration. [248]

Sumac 80% aqueous ethanolic extract had lipid lowering effect in high fat-fed rats. Examining heart tissue and injury biomarkers (serum aspartate aminotransferase and alanine aminotransferase) in liver, showed no adverse effects. [249]

Fruits 50% aqueous ethanolic, ethanolic and aqueous extracts were prepared and tested against TNF- $\alpha$ -induced inflammation in HaCat cells. Activity was measured with four biomarkers.<sup>[250]</sup>

A follow-up of previous research. Fruits were separately extracted with water, ethanol, 50% aqueous ethanol, acetone and ethyl acetate, and the TPC of each extract was determined. Extracts were tested for anti-inflammatory activity in *Helicobacter pylori* gastric epithelial cells. [251]

Aqueous extracts of ripe and unripe fruits had activity against twelve bacteria species. Fruits were separately extracted with 80% aqueous ethanol and 80% aqueous methanol. These extracts were active against *S. aureus*, *P. aeruginosa*, *E. coli*, *P. vulgaris*, *K. pneumoniae* and *B. subtilis*, with tetracycline as a reference. [253]

Sumac aqueous extract was added to ground sheep meat. It was active against *Listeria monocytogenes*, significantly reduced lipid peroxidation (TBARS) and controlled metmyoglobin formation. [254]

Sumac was successively extracted with n-hexane, chloroform, ethyl acetate, n-butanol, ethanol and water. These extracts were active against  $Staphylococcus \ aureus$ . in various concentrations. [255]

Sumac 80% aqueous ethanolic extract was active against  $E.\ coli.^{[256]}$ 

Sumac aqueous and ethanolic extracts were active against *S. aureus*, *E. faecalis*, *A. baumannii*, and *P. aeruginosa*. General chemical compositions are presented. [257]
Sumac (powder) was active against three bacteria species in fish aquariums. [258]

Sumac (from 22 locations) aqueous extract had activity against six bacteria species. It was analyzed for TFC and TPC, and its antioxidant activity was tested with DPPH method. [259]

Fruits were extracted with several solvents but only methanolic extract was used for antibacterial (six strains) and antioxidant (DPPH,  $\beta$ -carotene bleaching methods). Other extracts were used to determine general chemical composition. [260]

Fruits ethanolic extract had antibacterial (*S. aureus*, *B. cereus*, *E. coli* and *S. enteric*) and antioxidant (DPPH, method) activities. The major component (39.7%) of this extract was malic acid. [261]

Fruits EOs (hydrodistillation) from eight sources were tested for antibacterial (*S. aureus*, *E. coli*) and antioxidant (DPPH,  $\beta$ -carotene bleaching methods). In average, the major component of these EOs was  $\beta$ -caryophyllene. [262]

Fruits 80% aqueous and pure ethanolic extracts were tested against fourteen bacterial and fungal species, and their antioxidant activity was tested with DPPH method. In average, the major component of these extracts was fumaric acid. [263]

Fruits EO (hydrodistillation) and methanolic extract (ultrasonic-assisted) were prepared. Major component of EO was  $\beta$ -caryophyllene, while gallic acid was the major component of methanolic extract. Antioxidant activity of methanolic extract was determined with ABTS, DPPH and FRAP methods, its antimicrobial (ten bacteria and three fungi species) and its  $\alpha$ -glucosidase inhibition activity were also reported. [264]

Fruits from five locations (Iraq) were analyzed for TPC and nutritional composition. Their EOs (steam distillation) were tested for antioxidant (DPPH method) and antibacterial (*E*.

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coli) activities. In average, the major components of these EOs were Z,E-2,13octadecadien, caryophyllene oxide, 2,4-decadienal, E-caryophyllene and nonanoic acid.[265]

Fruits were separately extracted with *n*-hexane, dichloromethane (DCM), 70% aqueous methanol and water. Extracts were tested for enzyme inhibition (AChE, BuChE, DCM extract inactive), antioxidant (DPPH method) and antimicrobial (E. coli, S. aureus, P. aeruginosa and C. albicans) activities. [266]

Fruits aqueous extract was prepared and analyzed for general chemical composition, total anthocyanin content and TPC. It was tested for antibacterial (six strains), wound healing (mechanical cut of rats skin, measured by wound contraction and histochemical biomarkers), and antioxidant (myeloperoxidase concentrations) activities. [267]

Fruits 80% aqueous methanolic extract had antibacterial (eight species), antiparasitic (L. *major*, amastigotes and promastigotes). TPC and tannins content are reported. [268]

Seeds 95% aqueous ethanolic extract was analyzed affording four new compounds (Figure 6). These compounds were tested against three fungi species (A. flavus, C. albicans and P. citrinum) resulting no to significant activity. [269]

Fruits were separately extracted with acetone, ethanol, methanol and water. These extracts were active against two bacteria species: Pseudomonas syringae and Ralstonia solanacearum. Aqueous extract was analyzed for active components and eight of these were tested for the same activity, revealing 2,5-furandione as most active followed by malic acid, then coumalic acid (**Figure 6**). [270]

Fruits methanolic extract and its major component methyl gallate (Figure 2) were active against S. mutans. [271]

Fruits EO (hydrodistillation) was active against E. coli, P. aeruginosa, S. aureus and B. subtilis. The major components of this EO were (%): β-caryophyllene 34.3 and cembrene 23.8 (**Figure 6**). [272]

Leaves 60% aqueous ethanolic extract was active against B. subtilis, E. coli, K. pneumoniae, S. aureus and P. aeruginosa. Nine phenolics were isolated from this extract and characterized, including theaflavin and baccatune (Figure 6). [273]a

Sumac was supplemented to overweight volunteers resulting weight loss and insulin resistance lowering.<sup>[275]</sup>

Sumac was defatted with petroleum ether then extracted with 80% aqueous methanol, then fractionated with n-hexane, ethyl acetate and water. Extract and fractions were analyzed for TPC, and their antioxidant activities were tested with DPPH, sunflower oil oxidation and β-carotene bleaching methods. BHA and BHT were references. [276]

Fruits 70% aqueous ethanolic extract was prepared and fractionized with n-hexane, dichloromethane and ethyl acetate. Extract and fractions were tested for antioxidant activities with DPPH, H<sub>2</sub>O<sub>2</sub> (ROS against zebrafish embryos) and β-carotene bleaching methods. Crude extract and ethyl acetate fraction were most active. [277]

Fruits from fifteen genotypes were extracted with methanol and extracts were analyzed for general chemical compositions, TPC, total anthocyanin and tested for TAC. Analysis for organic acids resulted pentadecanoic and 9-octadecenoic acids as major components, and analysis for terpenes resulted  $\beta$ -caryophyllene and cembrene. [278]

Fruits were extracted with water in three different temperature and 50% aqueous ethanol. Extracts were analyzed for TFC, TPC, total anthocyanin content and tested for antioxidant activity with DPPH method. Analysis of extract showed that in average, gallic acid was the major component. [279]

Fruit powder inclusion in food of heat-stressed broilers had ameliorative effect, improved meat quality and increased meat antioxidant capacity (TBRAS method). [280]

Fruits 50% aqueous ethanolic extract was loaded into nanosheets that had wound healing

(deceasing wound closure time) and protection through antioxidant activity. The chemical composition of the extract included mainly organic acids and phenolics, where one of them was afzelin (**Figure 6**). [281]

Fruits powder supplementation (25 mg/d, 56 days) reduced blood pressure in patients with hypertension. [282]

Fruits 70% aqueous ethanolic extract had dose-dependent vasorelaxation activity on rat isolated aorta. A detailed mechanism of action is proposed. [283]b

Inclusion of fruits/seed powder in chicken/Fish diet improved their immune system, growth and egg/meat quality.  $^{[284-287]}$ 

Inclusion of seeds powder and exogenous fibrolytic enzymes, separately or combinedly (more active), increased wool length of male lambs.<sup>[288]</sup>

Adding fruits aqueous extract and lactic acid to commercial chicken wings increased their shelf life (storage time). [289]

Fruits aqueous extract had softening effect in cooked cattle chest meat. [290]

Inclusion of fruits powder in wheat bread improved its physical properties, antioxidant capacity (tested with DPPH method), and decreased salt amount needed to produce the same taste for humans.<sup>[291]</sup>

Fruits powder inclusion in stored fish meat extended its shelf life, physical properties and antioxidant activity (TBRAS method). [292]

Fruits 70% aqueous ethanolic extract supplemented to healthy mice had positive effect on their general health: body weight, blood sugar, blood lipids and blood triglycerides. [293]

Fruits powder supplementation to patients with non-alcoholic liver disease had positive effect on liver fibrosis, liver enzymes functioning, blood sugar, serum insulin and several other biomarkers. [294]

Fruits 70% aqueous methanolic extract was toxic to rabbits only in high dose of 5 g/kg. It had antidiarrheal effect against castor oil-induced fluid accumulation and diarrhea. In isolated jejunum, extract had relaxation effect of spontaneous and high  $K^+$ -induced contractions, with verapamil as a reference drug. [295]

Fruits 80% aqueous methanolic extract had analgesic effect in rats in three pain models (writhing test, tail flick test and formalin test). Aspirin and morphine were references. [296]

Fruits ethanolic extract had healing effect of wounds (mechanical cut) of rats. Effect was measured by wound contraction and biomarkers such as hydroxyproline and nitric oxide concentrations. [297]

- a- The presented structure of theaflavin in the article of G. Joseph  $et\ al.^{[273]}$  is incorrect, and the accurate name of "baccatune" is "baccatune A", according to the cited reference in the same article, namely T. Li  $et\ al.^{[274]}$  in our article.
- b- In the "Collection and Preparation of an Ethanolic Extract of *Rhus coriaria* Fruits" section of this article, it is said "The fruits of RC (Figure 1) were harvested ...". But viewing Figure 1 reveals that it does not include a photo of these fruits, and it does include four graphs.

# Rhus tripartite

Leaves were extracted with 80% aqueous ethanol and extract was analyzed for TFC and TPC, and its antioxidant activity was determined with DPPH and FRAP methods. Its antifungal activity was tested against *P. digitatum*. <sup>[128]</sup>

Leaves extract had allelopathic activity against several plants species. [298]

Leaves 70% aqueous acetone and 70% aqueous methanol extracts were prepared, and the second was fractionized with 50% aqueous n-butanol to obtain saponin-rich extract. Both extracts (acetonic and saponin-rich) had apoptotic effect in THP-1 cells. [299]

Roots 50% aqueous methanolic extract was active against castor oil-induced diarrhea in rats, and against diarrhea-causing bacteria (*S. aureus*, *E. coli*, *S. typhimurium*). [300]

Aerial parts were separately extracted with 70% aqueous acetone, 70% aqueous methanol and 70% aqueous ethanol. The following properties were determined using one or more of these extracts: analysis for TFC, TPC and general chemical compositions; antioxidant activity (DPPH, FRAP methods); antiproliferative activity (against CaCo-2, K-562 cells); anti-inflammatory activity (albumin denaturation method) and AChE inhibition. The major component of the aqueous-acetonic extract was rutin. [301]

Leaves, roots and stems were separately extracted with 50% aqueous methanol. The extracts were tested for antioxidant (ABTS, DPPH, FRAP, TAC methods), antimicrobial (five bacteria and two fungi species) and anti-inflammatory (carrageenan-induced paw edema in rats) activities. TFC, TPC and total anthocyanins content were determined. [302]

Leaves methanolic extract had activity against propylparaben-induced reproductive toxicity in male rats. Activity was measured by four antioxidant and two anti-inflammatory biomarkers. [303]

Leaves were separately extracted with n-hexane, chloroform, ethanol, methanol and water. Extracts were tested against twelve bacteria species where activity ranged from moderate to strong. [304]

Leaves 70% aqueous ethanolic extract was prepared and fractionated with ethyl acetate, *n*-butanol and water. Ethyl acetate was analyzed for chemical composition resulting several known saponins and phenolics. The crude extract was tested for antioxidant (DPPH method), antimalarial (against *Plasmodium falciparum*, with chloroquine as a reference) and antibacterial (against *S. aureus*) activities.<sup>[305]</sup>

Aerial parts were separately extracted (ultrasound-assisted) with 95% aqueous ethanol and chloroform. Extracts were tested for antioxidant (DPPH,  $\beta$ -carotene bleaching methods) resulting higher activity of hydroethanolic extract. Analysis of this extract obtained sakuranetin (**Figure 7**) as a major component. *Rhus retinorrhoea* which is not native to the reviewed region was also studied in this research. [306]

EOs (hydrodistillation) of aerial parts from seven locations (Algeria) were tested against five bacteria species. Analysis of these EOs revealed that in average,  $\alpha$ -pinene was the major component. [307]

Stems 80% aqueous methanolic extract was prepared and fractionized with ethyl acetate, dichloromethane and *n*-butanol. The crude extract had protective activity against isoproterenol-induced cardiotoxicity in rats. Activity was observed by measurements of oxidative/antioxidative biomarkers. Analysis of the crude extract resulted in isolation of several known compounds, including 3',8-binaringenin (**Figure 7**) that was isolated from this plant for the first time. [308]

Fruits were defatted with petroleum ether, then extracted with 70% aqueous ethanol and extract was fractionized with ethyl acetate. The remaining phase was considered aqueous extract. Extracts were analyzed for TFC, TPC, total tannins and tested for antioxidant activity (DPPH, FRAP, TAC methods). Qualitative phenolics composition of the hydroethanolic is presented. [309]

Aerial parts 70% aqueous methanolic extract was prepared and fractionated with ethyl acetate, *n*-butanol and water. Extract and fractions were analyzed for TFC, TPC and tannins content and were tested for antioxidant activity with ABTS, FRAP and DPPH methods. The crude extract was analyzed for phenolic composition resulting know compounds: myricetin-3-*O*-glucoside, myricetin-3-*O*-rhamnoside, quercetin-3-*O*-glucoside and quercetin-3-*O*-rhamnoside. [310]

Fruits and leaves were separately and successively extracted with petroleum ether, ethyl acetate, acetone and water; and their EOs were prepared by hydrodistillation. Extracts were analyzed for TFC, TPC and tannins contentment, and their antioxidant activity was tested with FRAP, DPPH and β-carotene bleaching methods. Analysis of extracts for

phenolics resulted known compounds (rutin as major in leaves and apigenin in fruits), and for fatty acids resulted seventeen in fruits and fourteen in leaves. For EOs, the major component of leaves was  $\alpha$ -pinene (22.5%) and of fruits was ( $\delta$ )-3-carene (18.1%, **Figure 7**). [311]

Stem bark 80% aqueous ethanolic extract was prepared and fractionized with ethyl acetate. Analysis of extracts for phenolics resulted in isolation of two active compounds (3,5,13,14-flavantetrol-catechin and epicatechin-3-*O*-rhamnoside)<sup>a</sup> that had HepG2 cells growth promotion and anti-hepatitis B virus activity. [312]

Stem bark neutral, basic and acidic aqueous extract were used to produces dyes for textile. The effect of various factors such as temperature, time and pH, was studied.<sup>[313]</sup>

Leaves general chemical composition is presented. [314]

Roots methanolic extract major components were 9Z,12Z-octadecadienoyl chloride and 9E,12E-octadecadienoyl chloride, each 46.89% (**Figure 7**). [315]b

Stem bark 80% aqueous methanolic extract was prepared and fractionized with water, dichloromethane, ethyl acetate and *n*-butanol. Crude extract was analyzed affording ten phenolics, one of them was novel, rhuspartin (**Figure 7**), and both materials had cytoprotective effect against methylglyoxal-induced endothelial cell apoptosis and were tested for antioxidant activity with DPPH method. [316]c

Stems 80% aqueous methanolic extract was prepared and fractionized with water, dichloromethane, ethyl acetate and *n*-butanol. Crude extract was analyzed resulting five active compounds where two of them were epicatechin and taxifolin (**Figure 7**). Extract, fractions and both compounds were tested for enzyme inhibition (cyclooxygenase, AChE) and antioxidant (NO radical scavenging, DPPH method, superoxide anion scavenging, TAC method, ascorbic acid and BHT were references) activities. [317]

Stems 50% aqueous methanolic extract was analyzed for TFC, TPC and anthocyanin content. It had ameliorating effect in ethanol-induced gastric ulcer in rats. Ranitidine was reference in this research. [318]

Fruits, leaves and stem bark (7 locations in Tunisia) were separately extracted with methanol, and extracts were analyzed for TFC and TPC. They were tested for antioxidant activity with DPPH and FRAP methods.<sup>[319]</sup>

a- In this article, it is written in the title that these two compounds are novel. This is incorrect. These compounds were previously reported several times and even from the same plant. See an earlier publication by the same group<sup>[316]</sup>, and even there, they did not present them as new compounds.

b- In this article, chloroform was reported as one of the components of roots methanolic extract. To the best of our search efforts, we found no confirmation to this reporting in this plant or in any other plant of this family presented in our review article.

c- A mistake in the title "methylgloxal" instead of methylglyoxal.

#### Schinus terebinthifolius

Leaves aqueous extract had allelopathic effect on Bidens alba and Rivina humilis. [320]

Fruits, crushed or intact, had allelopathic effect on *Rhizophora mangle* and *Avicennia germinans*; *Sphaeroma quadridentata*, *Artemia salina*, *Ilyanassa obsoleta* and *Petrolisthes armatus* (very weak effect). [321,322]

Intact seeds had allelopathic effect on seed germination of *Pinus palustris*, *Pinus elliotii* and *Quercus virginiana*. [323]

Leaves 95% aqueous methanolic extract was analyzed for TFC and TPC and had activity against methyl methanesulfonate-induced DNA damages in in *Allium cepa* (onion) cells and in mice. [324]

Fruits EO (steam distillation) was tested for anticancer (MCF-7 cell lines) and antioxidant (ABTS, DPPH methods) activities. It was analyzed for chemical composition and the

major compounds were (%):  $\alpha$ -phellandrene 35.16,  $\beta$ -phellandrene 10.81 (**Figure 8**) and  $\gamma$ -cadinene 18.26. In this research *Schinus molle* which is not native to the reviewed region, was also studied. [325]

Leaves ethyl acetate extract was analyzed for TPC and qualitative chemical composition. Its antioxidant activity was tested with DPPH and lipoperoxidation methods and it was tested for cytotoxicity in L929 fibroblasts. The anti-inflammatory activity was tested with 12-O-tetradecanoylforbolacetate-induced ear edema in mice, and with myeloperoxidase activity assay. [326]

Stem ethanolic extract was active against *C. tropicalis* with nystatin as a reference. [327]

Leaves lectin had activity against five bacteria and a fungal species. It was tested for carbohydrate-binding property (haemagglutinating activity) in glutaraldehyde-fixed rabbit erythrocytes. [328]

A follow up of the research cited in ref. 327, but in this the kinetics of the activity against *C. albicans* was studied. [329]

Stem 80% aqueous methanolic extract was active against B. subtilis, E. coli, E. amylovora, R. solanacearum and P. carotovorum. [330]

Leaves were separately extracted with n-hexane, toluene, ethanol, methanol, cold water and hot water. All extracts were tested against two different strains of Agrobacterium tumefaciens, resulting activity order of extracts: n-hexane  $\sim$  toluene < ethanol < hot water. [331]

Bark aqueous extract was active separately or combinedly (higher activity) with nystatin against four *Candida* ssp. (*C. albicans*, *C. krusei*, *C. glabrata*, *C. tropicalis*). [332]

Leaves 70% aqueous ethanolic extract had antiseptic effect on cows mammary quarters (udders) before and after milking, with commercial antiseptic iodine as a reference. [333]

Commercial ethylene glycol extract (plant part is not indicated) was active against for *Candida* ssp. (*C. albicans*, *C. dubliniensis*, *C. glabrata*, *C. Krusei*) in planktonic cultures and biofilms. [334]

Leaves EOs (fresh and dried, steam distillation), dichloromethane and 95% aqueous ethanolic extract were prepared and they were analyzed for TPC. Their antioxidant (DPPH,  $\beta$ -carotene bleaching methods) and antimicrobial (four bacteria and three fungi species) activity was tested. The chemical compositions of EOs were analyzed and many differences were detected, qualitatively and quantitatively. For example, the major component of fresh leaves EO was cis- $\beta$ -terpineol 17.87% (3.56% in dried leaves EO), while the major component of dry leaves EO was geranyl-n-butyrate 12.21% (0.51% in fresh leaves EO). See **Figure 8**. [335]

Leaves EO (hydrodistillation) was tested for antioxidant ( $\beta$ -carotene bleaching method) and antimicrobial (twelve bacteria and four fungi species) activity was tested. The chemical composition of this EO was analyzed and the major components were sabinene 40.66% and  $\alpha$ -pinene 30.27%. [336]

Fruits, leaves, stems and stem bark were separately extracted with ethanol and extracts were analyzed for TPC, and tested for antioxidant (DPPH method) and antibacterial (against *E. faecalis*). General chemical composition is presented. [337]

Leaves EO (hydrodistillation) and ethanolic extract was prepared in the traditional method and with ultrasonic assisted extraction, and the three materials were analyzed for TFC and TPC. Both extracts and five of their major phenolic components were tested for antioxidant activity by DPPH method, with BHT as a reference. EO and extracts were tested for antimicrobial (two bacteria and one fungus) activity, where ultrasonic extract was most active. EO major component was  $\delta$ -3-carene (68.78%). [338]

Leaves EOs (hydrodistillation), chloroform and methanolic extracts were prepared, as well as twigs EO. Both EOs were analyzed for fatty acids resulting fourteen in leaves and

thirteen in twigs. EOs were tested against four bacterial species (reference: ampicillin) and for antioxidant activity using DPPH method, and in both tests leaves EO was more active. In both EOs,  $\alpha$ -phellandrene was major component (33.06% leaves, 36.18% twigs). [339]

EOs (hydrodistillation) of fruits, leaves and twigs were prepared, analyzed for TPC, tested for antioxidant (DPPH, FRAP and  $\beta$ -carotene bleaching methods) and antibacterial (against five bacterial strains). The major components of these EOs were (%):  $\gamma$ -gurjunene 16.85 leaves (**Figure 8**),  $\beta$ -pinene 43.34 fruits and germacrene D 20.41 twigs. [340]

Leaves 80% aqueous methanolic extract was prepared and partitioned with n-hexane, dichloromethane, and ethyl acetate. Four active compounds against *Paraccocidioides brasiliensis* were isolated from this extract, with two standard antibiotics as references. One of these compounds is new (**Figure 8**). [341]

Fruits and leaves were separately extracted with 90% aqueous ethanol, and extracts were fractionized with *n*-hexane, dichloromethane, ethyl acetate and water. All ten materials were tested against *S. terebinthifolius*, *E. coli*, *S. aureus*, *C. neoformans* and *C. albicans*. Analysis of extracts and fractions for active compounds revealed the presence of nine fatty acids and other compounds that were previously presented. [342]

Industrial residues (mainly leaves and some fruits) were successively extracted with n-hexane, dichloromethane and methanol, and fruit peels were extracted with 54% aqueous ethanol. All extracts were tested against four bacteria species and analyzed for chemical compositions. Very detailed data is provided. [343]

Aerial parts EO (hydrodistillation) was tested against *E. coli*, *P. aeruginosa*, and *S. aureus* strains. The major components of this EO were (%):  $\alpha$ -pinene 24.3,  $\beta$ -myrcene 13.7 and  $\gamma$ -muurolene 16.6 (**Figure 8**). [344]

Leaves EO (hydrodistillation) was tested against nine *Staphylococcus* isolates and tested for toxicity in mice. It is indicated that acute toxicity was low but accurate value is not provided. Major components of this EO were *p*-cymen-7-ol 22.5% and 9-epi-(E)-caryophyllene 10.1% (**Figure 8**). [345]

Green fruits EO (hydrodistillation) was prepared and tested for antimicrobial (against three bacterial and seven fungal species and ssp.), anticancer (eight cell lines, and one non-tumor cells) and cytotoxic (against RAW 264.7 macrophages) activities. The major components of this EO were  $\alpha$ - and  $\beta$ -phellandrene. [346]

Dry leaves and their lipid extract were used to prepare a gel that had activity against S. aureus, E. coli and A. niger. In this gel, Ziziphus jujuba fruit powder was also used. In addition, aqueous and ethanolic extracts had the same activity. [347]

Fruits aqueous extract was prepared and fractionized with *n*-hexane, ethyl acetate and methanol. All materials were analyzed for active compounds against skin infections caused by *S. aureus*, resulting three previously presented triterpenoid acids. [348]

EOs (hydrodistillation) of ripe and unripe fruits, flowers and leaves from female and male trees were prepared (six EOs), and some of them were tested for antioxidant activity using DPPH and ORAC methods. The major components of these EOs were (%): terpinene-4-ol 24.1 female unripe fruits, sabinene 31.39 female ripe fruits,  $\alpha$ -pinene 21.25 female leaves,  $\beta$ -caryophyllene 20.64 male leaves and  $\alpha$ -pinene 32.49 male flowers. [349]

Fruits 10% aqueous methanolic extract was prepared, analyzed for TFC and TPC, and tested for antioxidant activity with DPPH method. One of its fractions that resulted from analysis for phenolics, had hypotensive effect in rotarod-induced hypertension in rats. [350]

EOs (hydrodistillation) of fruits and leaves were prepared and tested for antioxidant (DPPH method) and insecticidal (against *Sitophilus oryzae*) activities. The major components of these EOs were (%): limonene 23.22 in leaves EO and  $\alpha$ - and  $\gamma$ -terpinene 6.7 for each, in fruits EO. In this research *Schinus molle* that does not grow in the reviewed region was also studied. [351]

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Fruits EO (hydrodistillation) attenuated scopolamine-induced memory damage in zebrafish, and effect was measured by several behavioral tests and concentrations of AChE and other biomarkers (oxidant/antioxidant). The major components of this EO were (%):  $\beta$ -phellandrene 32.40,  $\alpha$ -pinene 16.68 and terpinen-4-ol 11.10. [352]

Leaves methanolic extract was fractionized with *n*-hexane, dichloromethane, ethyl acetate and water, and all materials were analyzed for active phenolic compounds against *Meloidogyne incognita* (root-knot nematode). Nine known compounds were isolated. [353]

Aqueous bark extract alleviated immobilization-induced ulcer in rats/mice. Effect was measured with pH and volume of the gastric contents, gastric hemorrhage and decrease in intestinal transit. In this research, *Myracrodruon urundeuva* (Anacardiaceae) that does not grow in the reviewed region, was also studied. [354]

Leaves EO (hydrodistillation) major components were  $\alpha$ -pinene,  $\beta$ -pinene,  $\gamma$ -carene and  $\alpha$ -phellandrene. [355]

In addition to were  $\alpha$ -pinene,  $\beta$ -pinene,  $\alpha$ -phellandrene and  $\beta$ -phellandrene as major components, three spirocyclopropane-type sesquiterpenes (**Figure 8**) were isolated from fruits EO (hydrodistillation). [356]

Exocarp was extracted with ethanol/water/acetic acid: 70:25:5 (v/v/v) and the extract was analyzed for phenolic composition, resulting mainly anthocyanins, including a novel one, 7-O-methylpelargonidin 3-O- $\beta$ -D-galactopyranoside (**Figure 8**). [357]

The kinetics of fruits and leaves EOs (hydrodistillation) preparation was studied revealing clear time dependent compositions. For example,  $\alpha$ -pinene and  $\beta$ -caryophyllene were the major components after 6 h, respectively, while tricyclene (**Figure 8**) consisted 8.3% of leaves EO and was not detected in fruits EO. After 4h, tricyclene consisted 24.1% of leaves EO and was the major component. As for fruits EO, if the preparation is ended after 1h,  $\alpha$ -trans-bergamotene (**Figure 8**) will not be detected, but after 6h it will consist of 5% [358]

Fresh leaves from nine locations were extracted with 80% aqueous ethanol and extracts were analyzed for chemical compositions. Major components varied according to location but in average, four compounds were with highest concentrations:  $\alpha$ -pinene, D-limonene,  $\gamma$ -carene and  $\alpha$ -phellandrene. [359]

General chemical composition of hulls ethanolic extract is presented. [360]

Phenolic compositions of bark 70% aqueous extracts (10 locations) are presented. [361]

Fruits (5 locations) EOs (hydrodistillation) were analyzed and in average, the major components were  $\alpha$ -pinene, D-limonene,  $\beta$ -pinene and  $\alpha$ -Copaene (**Figure 8**). [362]

Fruits (two locations) EOs (hydrodistillation) was analyzed and in average, the major components were  $\alpha$ -pinene, dl-Limonene,  $\rho$ -cymene, l-phellandrene, sylvestrene (**Figure 8**). EOs had cytotoxic activity against HL-60 and SK-MEL-28 cell lines. [363]

Fruits commercial EO was used in lambs diet as a substitute for antibiotic monensin. It also improved meat quality. [364,365]

Fruits were separately extracted (microwave-assisted) with ethanol and acetic acid and extracts were analyzed for TPC and qualitative compositions. They had positive effects of color preservation of caned sardines and metmyoglobin reducing activity. [366]

Bark ethanolic extract had alleviating effect against stomach incision in rats. [367,368]

Leaves aqueous extract synergistically with linoleic acid, reduced melanin synthesis in B16 cells and reconstituted epidermis (anti-hyperpigmentation). [369]

Fruits EO (hydrodistillation) had insecticidal activity against *Stegomyia aegypti* and antifungal activity against *Salmonella typhimurium*. The major components of this EO were (%):  $\delta$ -3-carene 55.43%, a-pinene 16.25 and sylvestrene 10.67. [370]

Leaves aqueous extract had insecticidal activity against Aedes aegypti larvae. [371]

Leaves 92% aqueous ethanolic extract had insecticidal activity against *Sitophilus* ssp. [372] Unripe fruits EO (hydrodistillation) and mixtures of some of its major components had insecticidal activity against Rhyzopertha dominica. The pure compounds that were used are (E)-nerolidol (**Figure 8**), limonene,  $\alpha$ -terpineol,  $\beta$ -terpineol, terpinolene,  $\alpha$ -pinene and β-pinene.<sup>[373]</sup>

Bark 70% aqueous ethanolic extract had insecticidal activity against female ticks of Rhipicephalus Boophilus microplus and their larvae hatchability. [374]

Fruits and leaves EOs (hydrodistillation) were applied against *Aedes aegypti*. The EOs were analyzed and the major components were bicyclogermacrene (27.57%) for leaves and  $\beta$ -pinene (30.32%) for fruits. [375]

Bark 70% aqueous ethanolic extract was not toxic for rats, administered in a single dose, indicated by measurement of many biomarkers. [376]

Bark aqueous extract had toxic potential in rats if administered chronically. [377]

Lectin isolated from leaves had healing activity of S. aureus infected wounds in rats by reduction of inflammation. Effect was measured by wound contraction, cell debris and several inflammatory biomarkers. [378]

# Searsia pentaphylla

Fruits, leaves and stem bark (2 locations in Tunisia) were separately extracted with methanol, and extracts were analyzed for TFC and TPC. They were tested for antioxidant activity with DPPH and FRAP methods. [319]

Fruits 80% aqueous methanolic or acetonic extracts had anticorrosion activity in carbon steel that was found in 1 M HCl solution. Methanolic (contains 1% HCl) extract was analyzed and eleven phenolics were detected, where two of them are not specified isomers of kaempferol hexose malic acid. An isomer of this structure is presented in **Figure 9**. [379]

Ripe and unripe fruits were separately ultrasonic-assisted extracted and extracts were analyzed for TFC, TPC and condensed tannins contents. The antioxidant (DPPH, FRAP methods) and antimicrobial (four bacteria and a fungi species) activities are reported. [380]

Fruits and leaves were separately extracted with ethanol and extracts were analyzed for TPC. Their antioxidant (DPPH, FRAP methods, BHT and quercetin were references) and antinociceptive (hot plate, writhing and formalin tests, in mice, morphine was reference) activities were tested. [381]

Fruits and leaves aqueous extracts were prepared and analyzed for general chemical composition, TFC and TPC. Their antioxidant (DPPH, FRAP, β-carotene bleaching methods) and in vitro anti-platelet aggregation (isolated from rats blood) activities. [382]

Aerial parts EO (hydrodistillation) and the hydrosol were tested for antioxidant activity using DPPH and FRAP methods. They were analyzed for TFC, TPC and chemical compositions, resulting hexadecanoic acid (31.5%) and spathulenol (14.9%) in EO, and spathulenol (14.2%) in the hydrosol. [383]

Aerial parts ethyl acetate and methanolic extracts were prepared and tested for antioxidant (DPPH, FRAP, β-carotene bleaching, hydroxyl radical scavenging methods) and AChE inhibition activities. They were analyzed for phenolic compositions resulting known compounds (10 for ethyl acetate extract and 9 for methanolic) like the glycoside epimers astragalin and hyperoside (Figure 9). [384]

Bark aqueous extract was used as efficient wool colorant. [385]

Leaves aqueous extract was found non-toxic for mice, had hypotensive effect in rats and vasorelaxant effect on aorta isolated from rats. Mechanisms of action are presented. [386]

Figure 2: Natural products isolated from Pistacia atlantica.

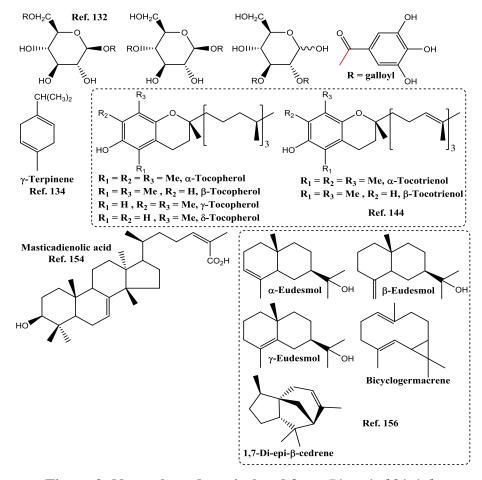


Figure 3: Natural products isolated from Pistacia khinjuk.

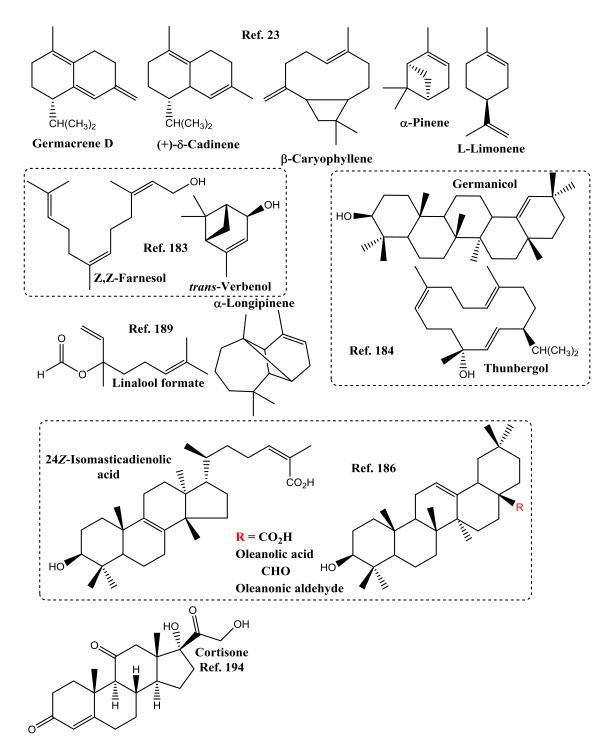


Figure 4a: Natural products isolated from Pistacia lentiscus.

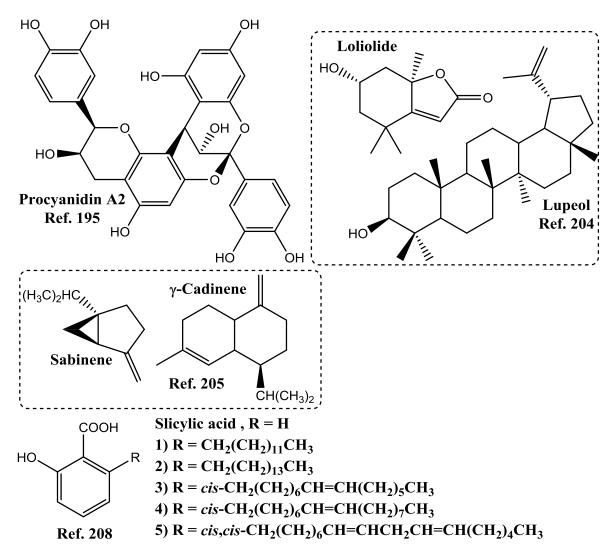


Figure 4b. Natural products isolated from *Pistacia lentiscus*.

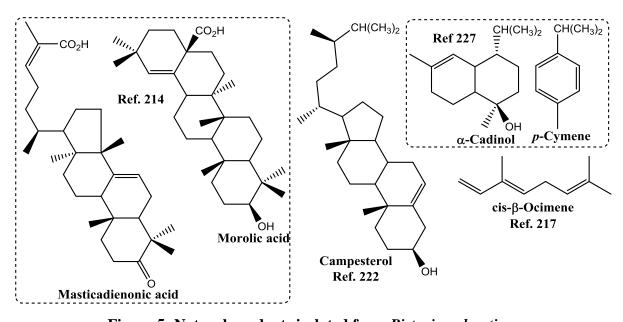


Figure 5: Natural products isolated from *Pistacia palaestina*.

Figure 6: Natural products isolated from Rhus coriaria.

Figure 7: Natural products isolated from Rhus tripartite.

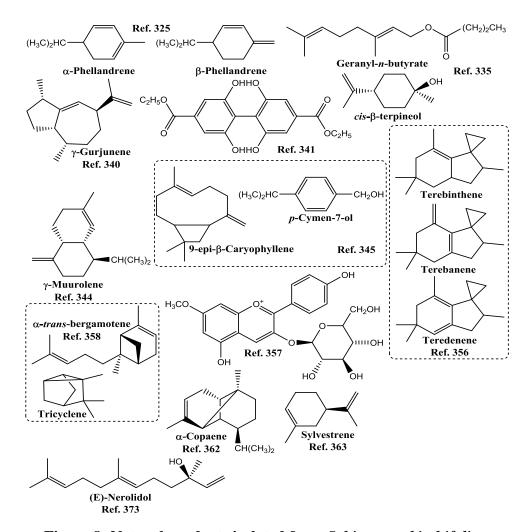


Figure 8: Natural products isolated from Schinus terebinthifolius.

Figure 9: Natural products isolated from Searsia pentaphylla.

#### 4. DISCUSSION

In the introduction of this article, we mentioned that in the reviewed region, the landscape between the Mediterranean sea and the Jordan river, eight wild plants of the Anacardiaceae are found: *Pistacia atlantica*, *Pistacia khinjuk*, *Pistacia lentiscus*, *Pistacia palaestina*, *Rhus coriaria*, *Rhus tripartita*, *Schinus terebinthifolius* and *Searsia pentaphylla*. All these trees are known to the regions peoples since ancient times except *Schinus terebinthifolius*, that there is no controversy that its origin is South America. It is known in Israel and Palestine as well as all the world by the common name of "Brazilian pepper tree". It is agreed among most scholars that this tree was introduced to the reviewed region after its introduction in Europe, but it is not clear how and when the introduction from Europe occurred. In many regions such as the USA and South Africa, *S. terebinthifolius* is considered invasive problematic plant. However, this is not the case in our reviewed region where its wild distribution is relatively limited but it can be easily found in gardens as ornamental plant.

*Pistacia atlantica* is one of the most studied among the eight species of this family in the reviewed region. In addition to numerous studies of its chemical composition, that we will furtherly discuss here, this species has a special economic importance as turpentine source. <sup>[389]</sup> This mixture of volatile compounds such as  $\alpha$ -pinene, is prepared by extraction of the tree gum, which is obtained by making wounds in the tree trunk. The turpentine prepared from *P. atlantica* is achieved in lower amounts compared to pine trees, but is chemical composition is richer and it is more aromatic.

This richness was extensively investigated for gum, resin, essential oils of all parts as well as their extracts, and this was extensively presented in **Table 2**. But this research still has major interest of researchers. One of the very recent examples was published by N. Belyagoubi-Benhammou ahc, who studied obtained EOs and 60% aqueous methanolic extracts of male

buds, female buds, male roots, female roots, ripe and unripe fruits from three locations in Algeria. [390] In this comprehensive publication, they reported the chemical compositions, TFC, TPC and antioxidant activity of these materials. All detected compounds, phenolics and EOs components are previously known, but some findings should draw additional attention. In average, the major detected phenolic compound was hydroxytyrosol, and in EOs, after major fatty acids, anacardol (3-(8-pentadecenyl)phenol) and *n*-tetradecanol were observed (**Figure 10**). They conclude that these materials have nutritional, industrial and cosmetic values.

Figure 10: Natural products isolated from *Pistacia atlantica*. [390]

Most extracts and EOs are prepared from dried plant matter. So, as it has been published in very large number of studies, the drying process has major influence of the quantity and the quality of the resulting materials. N. Yaramadi ahc investigated the effect of different drying conditions of *P. atlantica* on many properties of the plant matter.<sup>[391]</sup> After drying, the extraction process has a crucial effect on the resulting EOs and extracts. M. Salhi ahc studied the influence of three EO preparation methods on several properties of these Eos. [392] They prepared seeds EOs by cold press, n-hexane extraction and by super-critical-CO<sub>2</sub> extraction and analyzed general chemical compositions (many compound families), TPC and tested their antioxidant activities (three methods). They found significant differences in all these properties. For example,  $\alpha$ -tocopherol was the major components of this compound family  $(\alpha, \beta, \gamma)$  and  $\delta$ -tocopherol were detected), and its concentrations in the three EOs were (mg/kg): 69.04 cold press, 64.9 *n*-hexane extraction and 73.52 super-critical-CO<sub>2</sub> extraction. It is also important to mention that the quality and quantity of plant products are also a result of circumstances that sometimes humans have no control of them, especially for wild plants. In this context, H. Benhassaini ahc showed that salt stress on P. atlantica has clear influence on proline and soluble sugar accumulation in the plant. [393] In this case, experiments were performed with cultivated plantlets.

Many of the active ingredients of *P. atlantica* were studied for biological-medicinal activities *in silico*, *in vitro* and *vivo*, in animal and human models. One of the recent works was published by N. Taib ahc, where they performed molecular docking of some of these compounds against main protease of SARS-CoV2 virus. These compounds were  $\beta$ -eudesmol, (*trans*)verbenol, both shown in previous figures, and elemol, pinocarvone, myrtenal, *trans*-carveol, and *trans*-pinocarveol was found inactive (**Figure 11**). Interestingly, in the abstract of this publication and in two tables, verbenol is mentioned but the docking image shows verbenone.

Figure 11: Natural products in *P. atlantica* with anti-SARSCoV2 potential. [394]

Nanoparticles gained great importance almost in all fields of science and industry, and their importance for drug development and therapy was published in a very large number of articles.<sup>[395]</sup> For the purpose of this review article, there are four types of nanoparticles that plant materials are related to: nanoparticles of plant materials themselves, plant materials are loaded on/in nanoparticles, metal/metal-oxide nanoparticles that were obtained via "green synthesis" using plant materials, in the vast majority of cases, these are aqueous extracts. In **Table 3**, a summary of published nanoparticles and their activities, that are related to Anacardiaceae species of the reviewed region.

Table 3: Activities of nanoparticles (NPs) related to Anacardiaceae species.

Species/Plant Material	NP	Activities/Reference
P. atlantica, bark aqueous extract	Ag	Anti-gastric cancer <sup>[396]</sup>
P. atlantica, EO loaded on		Anti-breast cancer <sup>[397]</sup>
P. palaestina, fruits aqueous extract	Ag	Wound healing <sup>[398]</sup>
R. coriaria, fruits aqueous extract	Ag	Anticancer, MCF-7 cells <sup>[399]</sup>
R. coriaria, fruits aqueous extract	Ag	Antimicrobial, DNA protective <sup>[400]</sup>

The scientific name of *Pistacia khinjuk* originates from the tree name in Balochi language spoken in Baluchistan region, which is generally an arid habitat. Even though this species is well adapted to this environment, controlled studies by A. Ranjbarfordoei revealed that under

drought stress, there is an increase of chlorophyl production by the plant.<sup>[401]</sup> The research included *P. atlantica* that they name as *P. mutica*, which was less adaptable to these conditions. In a follow-up study, the same group investigated the effect of drought and salinity (NaCl) combination of the two species and reached the same result: *P. khinjuk* is more adapted that *P. atlantica*.<sup>[402]</sup>

Compared with other *Pistacia* species reviewed in this article, seeds EO of *P. khinjuk* was not reported so far. M. Ahmadi and F. Karimi published an enzyme-assisted extraction method, where they used composite design with protease and  $\alpha$ -amylase, separately. [403] After optimization of extraction conditions (incubation time, temperature and pH), they achieved high yields. Three years later, the same group published a follow-up research with improved methods supported by theoretical analysis. [404]

F.K. Hammoud ahc prepared activated carbon from the fruit hulls of *P. khinjuk* which had high adsorption capacity, low density, low ash content and low humidity. [405] S. Asif ahc used nonedible seeds EO that was prepared by extraction with *n*-hexane, to synthetize biodiesel by ultrasonic-assisted methylation. [406] In a similar EO preparation method, V. Karthickeyan ahc esterified this EO to produce biodiesel, and they studied its chemical composition and combustion qualities. [407] To conclude this part, we will present the work of B. Hosseinzdeh Samani ahc that prepared biodiesel from EO of *P. atlantica* in the same method of S. Asif, but this research was performed two years earlier and reported higher yields. [408] This is probably a result of higher EO content in seeds of *P. atlantica* compared with *P. khinjuk*.

A very interesting work was recently published by A.L. Stefi ahc about changes that occur in the compositions of *Pistacia lentiscus* young trees, as a result of external parameters: heat and cold stresses.<sup>[409]</sup> In addition to morphological changes, this research showed that the differences between the effects of heat and cold are very significant, compared to each other, and compared to control trees that were not under stress. These changes are summarized in **Table 4**.

Table 4: Effects of heat and cold stresses on *P. lentiscus*, A.L. Stefi ahc. [409]

Measured Change	Heat Stress	Cold Stress
Cumulative biomass	slight decrease	large decrease
Oxidative stress	very large increase	large increase
Leaf pigments absorbance	no change	no change
Dopamine concentration	very large increase	large increase

Phenethylamine concentration	slight decrease	slight decrease
Phenylalanine concentration	very large increase	slight decrease
Tryptophan concentration	large increase	slight increase
Tyramine concentration	slight increase	slight decrease
Tyrosine concentration	very large increase	no change

The stage of ripening or maturity has a vital role in determining the chemical composition of plants materials, especially the fruits, and **Table 1** includes many examples. K. Boudieb ahc analyzed the chemical compositions and tested antioxidant activities of ripe and unripe fruits EOs (cold extraction with *n*-hexane) and methanolic extracts of *P. lentiscus*. <sup>[410]</sup> They discovered significant differences in TPC, total anthocyanins content, color and antioxidant activity (DPPH, FRAP methods) of extracts. The compositions of EOs were also clear. For example, ripe fruits EO contained oleic acid-3-hydroxy-*n*-propyl ester and unripe EO did not, while unripe fruits EO contained methyl cholate (**Figure 12**) but ripe fruits EO did not.

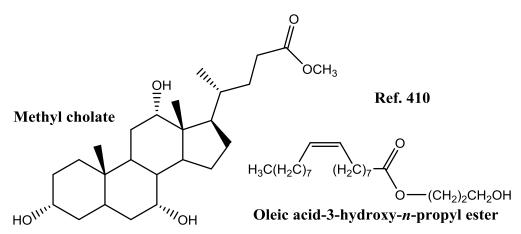


Figure 12: Natural products in *P. lentiscus* ripe and unripe fruits Eos. [410]

A more comprehensive work was published by S. Dragovic ahc where they tested the effects of climate conditions, growth location, maturity stage and extraction solvent on 80% aqueous methanolic and aqueous ethanolic extracts, and they report some differences.<sup>[411]</sup>

Sustained release is a very important method in drug delivery, and R.M. Goda and M.M. Shohayeb used it in preparation of silicon urinary catheters. This was done for the treatment of bacterial colonies with benzoic acid or cholesterol, that were sustain-released from coatings prepared with *P. lentiscus* resin extracts (aqueous, ethanolic and ethyl acetate). *Pistacia palaestina*, that has many synonym scientific names, was thoroughly investigated for the effect of various factors on its composition and products, like extracts and EOs. These include growth conditions, maturity stage and extraction method. S. Gülsoy ahc studied the

effect of locality (environment, 17 locations) on the chemical composition of ripe fruits Eos. [413] Considering the concentrations of the four major components (α-pinene, myrcene, limonene and β-caryophyllene), the differences between these locations are notable, even though α-pinene is the major component in all of them. But reading all the data carefully reveals some great differences. For example, germacrene D is found only in the fruits EO from one location. In a very comprehensive research, W. Zam ahc studied the effect of drying methods, extraction temperature, extraction time and maturity stage on leaves extracts, prepared using 40, 60, and 80% aqueous methanol, ethanol and acetone. [414], see a note after this reference]. They analyzed these extracts these extracts for TPC and tested their antioxidant activity with DPPH, resulting clear differences. For example, using 40% aqueous acetone to extract mature leaves in four extraction times (T = 40 °C), 15, 30, 45 and 60 min, TPC was (g/100 g) 18.21, 19.19, 18.85 and 17.61, respectively. M. Inan focused on the effect of seasonality (four stages) on the fatty acid composition of fruits petroleum ether extract. [415] Oleic acid was the major components of all these extracts that differed in their yields, but the second and third components were not the same in all four extracts. F. Kaya and A. Ozer studied, theoretically and experimentally, the effects of extracting solvent, extraction time and extraction temperature of the yields of seeds extracts.  $^{[416]}$  They used *n*-hexane, *n*-heptane, petroleum ether and carbon tetrachloride, 20-40 min and 40-98 °C, according to the solvent boiling point. In some cases, they found significant differences. For example, using  $CCl_4$  as extraction solvent for forty minutes, 56 or 76 °C, yields were 95.2 and 98.1%, respectively, compared with the theoretical expected yield.

K. Rand ahc found out that the chemical composition of leaves galls of *P. palaestina* produced by the effect of *Baizongia pistaciae* insect, is notably different of the intact leaves. [417] They found large differences in the total concentrations of mono- and sesquiterpenes, and also very large differences in the concentrations of single compounds. For example, the average concentration ( $\mu g/g$ ) of  $\alpha$ -pinene in intact leaves of five trees was 0.772, while in galls of the same trees leaves it was 103.24. In a follow-up study, this group found that not only the accumulation of monoterpenes is different in intact leaves and galls, but also the monoterpene synthase enzyme activity was entirely different: way higher in galls. [418] The group investigated the relationship between genes involved in the biosynthesis of natural products and the concentration changes in galls compared with leaves and calculated the fold increase, in two locations. [419] For example, the concentration of (+)- $\beta$ -pinene was 1.5 folds in one location and 45 folds in another. But the concentrations do not

always increase: the concentrations of (-)- $\alpha$ -cubebene are 0.06 folds in one location and 5 folds in the second; and for  $\beta$ -ylangene 0.12 and 0.3 folds, respectively (both compounds are shown in **Figure 13**).

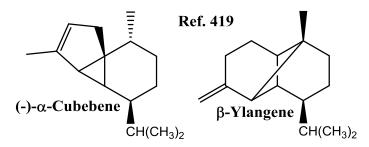


Figure 13: Natural products in *P. palaestina* leaves and galls. [419]

*Rhus coriaria* is one of the most important among the Anacardiaceae trees because of the spice prepared from the fruits, sumac. It is important to clarify that this name is given sometimes to the tree itself and even to other *Rhus* genus trees, but in the region between the Mediterranean sea and the Jordan river, the name sumac refers to the spice with crimson red color.

The chemical composition of *R. coriaria* has been extensively studied and published but there are still a few points to discuss. I.M. Abu-Reidah ahc from the Palestinian Authority, published a comprehensive investigation of the chemical composition of fruits 80% aqueous methanolic extract. [420] G. Lo Vecchio ahc separately extracted fruits from Sicily with *n*-heptane for fatty acids and with methanol for phenolic composition. [421] The first group reported qualitative very detailed composition while the second group reported quantitative composition of major compounds only. Although both groups used the same plant material and close polar solvents, their findings include major differences. G. Lo Vecchio ahc reported that the major component was hyperoside (quercetin 3-O-galactoside, **Figure 9**) with 160.54 mg/g, but in the publication of I.M. Abu-Reidah ahc this compound is not mentioned. This difference highlights the importance of locality in preparation and using plant materials. In addition to the mentioned extracts, G. Lo Vecchio ahc prepared several other extracts, tested antibacterial (seven strains) and zebrafish embryo acute toxicity.

N. Nayebpour and H.A. Asadi-Gharneh prepared petroleum ether extracts of fresh fruits from six different locations in Iran and analyzed them for fatty acids compositions. [422] Oleic acid was the major component in all samples but the concentrations of second and third acids, linoleic and palmitic, notably exchanged. M.A. Farag ahc used solid-phase microextraction to

analyze the chemical compositions of fresh fruits from Egypt, Jordan, Palestine and roasted fruits from Palestine. The differences were very significant, in compound families and single compounds, and these were presented in a very detailed fashion. For example, the concentration of  $\alpha$ -humulene (**Figure 14**) in these extracts was (%): 0.93, 1.48, 1.49, 1.29, respectively.

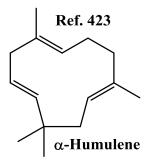


Figure 14: α-Humulene from *Rhus coriaria* fruits. [423]

M. Grassia ahc prepared *R. coriaria* fruits 50% aqueous methanolic extract and analyzed it for qualitative chemical composition. A very detailed list is presented.<sup>[424]</sup> They also tested the suitability of this extract for microencapsulation and discovered that this process was most successful when it was done with maltodextrin, where the bioavailability of the active ingredients was highest. Finally for this part, R. Kossah ahc analyzed fruits for nutritional ingredients and fatty acids composition and their findings were very close the results of N. Nayebpour and H.A. Asadi-Gharneh. [422],[425] In this research *Rhus typhina* was also studied, and a follow-up article was published a year later by the same group where they optimized the extraction processes. [426]

M.M. Feuereisen ahc performed pressurized liquid extraction of anthocyanins and biflavonoids from *Schinus terebinthifolius*, where they optimized temperature, time, solvent (ethanol) amount and acid concentration.<sup>[427]</sup> This resulted high yields of extracts. A research that was carried out by R. Acácio ahc found that microencapsulation of seeds EO, enhanced its stability and increased its bioavailability.<sup>[428]</sup> Finally, J. Wang ahc found out that inhalation of fruits EO by students, resulted was related physical sensations such as relaxation, sedation and improvement of breathing, but also discomfort in the respiratory system, such as nose stinging, in addition to psychological effects like memories and various positive feelings.<sup>[429]</sup>

## 5. Selected Activities of *Pistacia vera*

Among domesticated Anacardiaceae plants, *Pistacia vera* is the only tree that is very limitedly cultivated in the reviewed region of this article, but it is widely cultivated in neighboring Middle Eastern countries like Turkey and Iran. Compared with another globally cultivated tree of the Anacardiaceae family, Cashew (*Anacardium occidentale*), the global market of *P. vera* is significantly smaller: USDB 8 and 4.133, respectively [430,431]. Cashew is consumed in the region between the Mediterranean sea and the Jordan river but it is not cultivated there. Archeological studies found out that *P. vera* was used by humans as early as 300000 year ago<sup>[432]</sup> and was domesticated around 8000 years ago.<sup>[433]</sup>

Numerous articles were published about the chemical composition of *P. vera* and its biological activities. But since this article presents wild trees of Anacardiaceae family in the reviewed region, we will cite just two publications. M. Elakremi ahc studied the chemical composition, TPC and the antioxidant (ABTS, DPPH, FRAP methods) of 50% aqueous ethanolic extracts of female and male leaves and hulls. They reported 42 compounds including 1-methyl-1H-pyrrole (**Figure 15**) as a major component, in average. S. Safdar ahc prepared fresh fruits *n*-hexane, chloroform and ethanolic extracts and tested them for antibacterial (against *E. coli*, *K. pneumoniae*, *P. vulgaris*, *P. aeruginosa*, *S. aureus*, *S. epidermidis*) and anticancer (MCF-7, A2780 cell lines) activities. The chemical composition that they published is qualitative and it included some interesting compounds like 4,5-diamino-2-hydroxypyrimidine, *threo*-4-hydroxy-l-lysine lactone, N-methylpyrrole-2-carboxylic acid, 4-hydroxy-2-methylpyrrolidine-2-carboxylic acid, isosorbide dinitrate and 9-oximo-2,7-diethoxyfluorene (**Figure 15**).

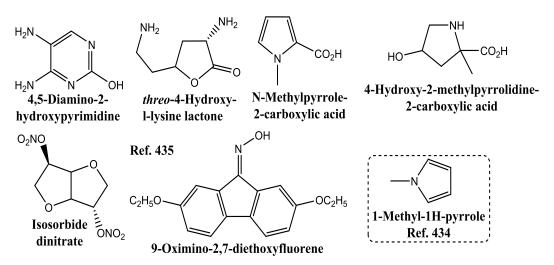


Figure 15: Natural products isolated from *Pistacia vera* extracts. [434,435]

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## 6. CONCLUSIONS

- 1) Anacardiaceae trees of Israel and Palestine possess important biological activities.
- 2) These plants contain natural products with unique structures.
- 3) These natural products should be studied for drug development and discovery.
- 4) The research of some of these species should be expanded.
- 5) Research should be done to extend products of these trees in cosmetics industry.

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