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Optimizing *Pistacia lentiscus* (mastic tree) food and healthcare applications: phytochemical composition, extraction methods, quality control, and novel delivery systems

Mohamed A. Anwar · Yuting Fu · Haroun Khan · Mohamed A. Farag

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Abstract *Pistacia lentiscus*, from the Anacardiaceae family, is native to the Mediterranean region and best known for its aromatic resin, Chios mastic gum (CMG), which is exclusively produced on Chios Island, Greece. While the gum is the tree's primary commercial product, various extracts from different *P. lentiscus* organs also hold potential applications due to their rich chemical profiles. This review assesses strategies to optimize the utilization of *P. lentiscus* products, not only the oleogum, in food and healthcare products. First, we review the phytochemical composition and environmental factors affecting this composition, highlighting conditions that maximize yield for different uses and applications. Additionally, various extraction techniques are reviewed, including solvent, ultrasonic-assisted, microwave-assisted, and supercritical fluid extraction methods, to identify the most effective methods. Authentication and quality control aspects, particularly for CMG, are compared, besides highlighting recent advances in novel delivery systems, i.e., liposomes, that are used to enhance the bioavailability of CMG key phytoconstituents.

M. A. Anwar · M. A. Farag (✉)
Pharmacognosy Department, Faculty of Pharmacy, Cairo University, Kasr El Aini St., P.B. 11562, Cairo, Egypt
e-mail: mohamed.farag@pharma.cu.edu.eg

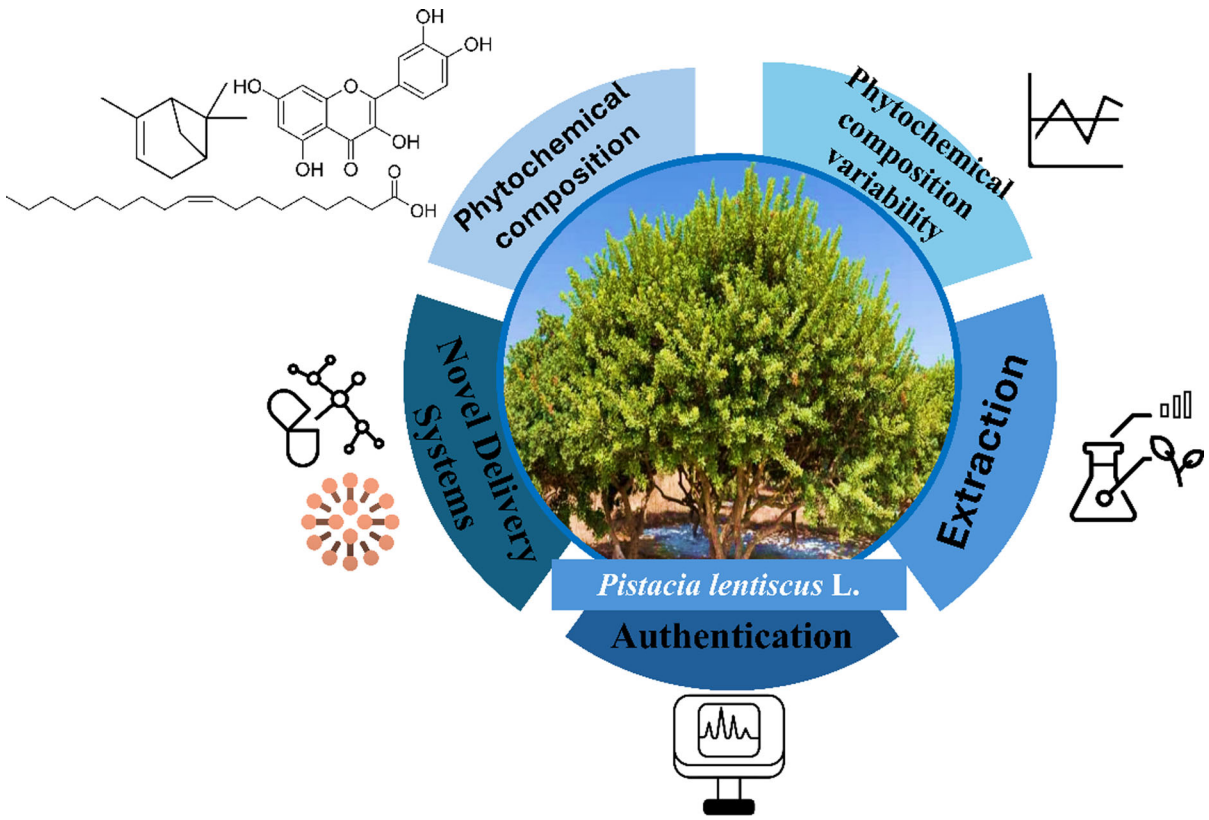
M. A. Anwar
e-mail: mohamed.anwar@pharma.cu.edu.eg

Y. Fu
Key Laboratory of Food Nutrition and Functional Food of Hainan Province, School of Food Science and Engineering, Hainan University, Haikou 570228, China
e-mail: 24110832000014@hainanu.edu.cn

H. Khan
Department of Pharmacy, Abdul Wali Khan University Mardan, Mardan 23200, Pakistan
e-mail: haroonkhan@awkum.edu.pk

H. Khan
Department of Pharmacy, Korea University, Sejong 20019, South Korea

Graphical abstract



Keywords *Pistacia lentiscus* · Chios mastic gum · Phytochemical variability · Extraction · Authentication · Delivery system

Abbreviations

AMGE	Acidic mastic gum extract
CMG	Chios mastic gum
CSE	Conventional solvent extraction
DES	Deep eutectic solvents
DM	Dry matter
DPPH	1,1-Diphenyl-2-picryl-hydrazyl
DW	Dry weight
ESI(+)-FT-ICR	Electrospray ionization-Fourier transform-ion cyclotron resonance mass spectrometry
GAE	Gallic acid equivalent
GC-FID	Gas chromatography-flame ionization detection
GC–MS	Gas chromatography–mass spectrometry
HD	Hydro-distillation
HPLC	High-performance liquid chromatography
HPLC-DAD	High-performance liquid chromatography-diode array detector
HPLC-ELSD	High-performance liquid chromatography-evaporative light scattering detector
HPLC-UV	High-performance liquid chromatography-ultraviolet detector
HPTLC	High-performance thin layer chromatography
HS-SPME-GC–MS	Head space solid-phase microextraction gas chromatography–mass spectrometry

HSV-2	Herpes simplex virus type 2
IC_{50}	Half maximal inhibitory concentration
IMNA	Isomasticadienonic acid
MAE	Microwave-assisted extraction
MNA	Masticadienonic acid
MUFA	Monounsaturated fatty acid
PCA	Principle component analysis
PDA	Photo diode array detector
PDO	Protected Designation of Origin
PUFA	Polyunsaturated fatty acid
SE	Solvent extraction
SFA	Saturated fatty acid
SFE	Supercritical fluid extraction
SPME–GC–MS	Solid-phase microextraction gas chromatography-mass spectrometry
RE	Rutin equivalent
TLC	Thin layer chromatography
TPC	Total phenolic content
UAE	Ultrasonic-assisted extraction
UFA	Unsaturated fatty acid
UHPLC-ESI–MS/MS	Ultra-high-performance liquid chromatography-electrospray ionization-tandem mass spectrometry
UHPLC-Q-Orbitrap-HRMS	Ultra-high-performance liquid chromatography coupled to quadrupole Orbitrap high-resolution mass spectrometry
UV	Ultraviolet

Introduction

The genus *Pistacia* from the family Anacardiaceae comprises about 20 species of flowering plants, including *Pistacia lentiscus,* which is famous for its medicinal applications and economical value (Bozorgi et al. 2013). *Pistacia lentiscus* L., commonly known as lentisk or mastic tree, is an evergreen deciduous shrub that grows to 5 m tall and spreads in the Mediterranean area (Milia et al. 2021; Yosr et al. 2018). Its popularity comes from the unique aromatic resin that is primarily produced by *P. lentiscus* trees on the southern part of Chios Island in Greece, and hence is known as Chios mastic gum (CMG) or simply mastic or Mastiha (Paraskevopoulou and Kiosseoglou 2016). Earlier studies referred to mastic-producing trees as *Pistacia lentiscus* var. *chia*; however, this term is no longer taxonomically accepted, and since 2015 the European Pharmacopoeia has adopted *Pistacia lentiscus* L. without cultivar or variety specification (Pachi et al. 2020).

Attempts to produce mastic gum outer Chios Island were characterized by limited success (non-existent resin or poor production). This arises from the specific ecological factors of Chios Island represented in a temperate climate, underwater volcanic zone, and thick calcaceous soil (Ierapetritis 2010; Paraskevopoulou and Kiosseoglou 2016). Thus, the European Union identified CMG as a Protected Designation of Origin (PDO) product since 1997 (Pachi et al. 2020). Some studies reported successful production of mastic gum in Turkish areas (Karaburun and Cesme peninsulas), which are geographically close to Chios (Sarikahya et al. 2024; Tabanca et al. 2020). Mastic trees start producing gum in the 5th year, with maximum yield (1 kilo) after the 12th year (Ierapetritis 2010). From July to September, mastic growers made vertical slits (from 20 to 100 slits, based on tree age) in the trees' trunks and branches to receive resin. After that, this resin remains exposed to the environment under trees for several days to coagulate and dry before collecting it by hand for further purification steps, such as sieving and washing (Paraskevopoulou and Kiosseoglou 2016). In 2014, UNESCO recorded the know-how of mastic cultivation on the island of Chios in the Representative List of the Intangible Cultural Heritage of Humanity (Pachi et al. 2020).

Traditionally, people in Greece used CMC for different conditions, including dyspepsia, stomach ulcer, oral health, and hypercholesterolemia (Bozorgi et al. 2013). Several studies have been reported on its biological activities, such as antioxidant, antimicrobial, anti-inflammatory, anticancer, wound healing, and cardioprotective effects (Soulaidopoulos et al. 2022). Chemically, the trans-1,4-poly-β-myrcene polymer is the base of CMG that keeps the bioactive compounds in the gum form. CMC possesses a wide range of metabolites belonging to various classes *viz.* triterpenes, volatile compounds (monoterpene and sesquiterpenes), alongside phenolic acids (Pachi et al. 2020). Because the gum flavor is linked with its essential oil, CMG or its oil is used as an ingredient in various food products, such as chewable gums,

desserts, and beverages (Paraskevopoulou and Kiosseoglou 2016). Also, CMG participates in other nonfood products, such as medical creams, toothpastes, perfumes, and paint varnishes (Pachi et al. 2020; Paraskevopoulou and Kiosseoglou 2016). According to a report by Global Market Insights (issued August 29th, 2025) on the mastic gum market, the market is projected to grow from an estimated USD 751.6 million in 2025 to USD 1,080.8 million by 2035, reflecting a compound annual growth rate (CAGR) of 3.7% over the period.

Besides CMG from the Chios Island, *P. lentiscus* trees, especially outside Chios, represent a source for other valuable products, such as leaves and fruits (Milia et al. 2021). Together with stems and roots, they yield essential and fatty oils as well as various extracts that are rich in volatile compounds; fatty acids, sterols, carotenoids, and tocopherols; and phenolics, respectively (Aissat et al. 2022; El Bishbishy et al. 2020; Harrat et al. 2020; Mezni et al. 2014a; Yosr et al. 2018). Literature reported various ethnomedicinal uses for these organs, such as leaves for curing jaundice, fruits as condiment and for scabies as well as stems and roots as antiseptics (Bozorgi et al. 2013). Different extracts of leaves and fruits showed various health-promoting activities exemplified in antioxidant, anti-inflammatory, antimicrobial, antidiabetic, and hepatoprotective actions (Sehaki et al. 2023), confirming the medicinal value of these extracts. Moreover, the distilled leaves (by-product leaves that have undergone a distillation process) represent a valuable source for phenolic compounds such as flavonol glycosides (Elloumi et al. 2022a, 2022b). In Tunisia alone, an annual production of 100 L of essential oil from *P. lentiscus* leaves may generate over 100 tons of solid waste per year (Elloumi et al. 2022a).

As the chemistry of CMG, leaf, and fruit were previously reported (Milia et al. 2021; Pachi et al. 2020; Sehaki et al. 2023). This review focuses mainly on studies from 2020 to 2025, with special emphasis on non-reviewed non-volatile constituents, i.e., fatty acids, sterols, and carotenoids from articles dating back to 2010. To maximize the production of *P. lentiscus* metabolites, the impact of the different factors, such as environmental conditions and extraction methods, on the yield and composition of various extracts is presented for the first time in the literature, and not only focused on gum but rather other organs' extracts. Approaches to confirm high-quality *P. lentiscus* products, alongside novel delivery systems of different extracts, are further reviewed. Numerous search engines and publication houses (PubMed, Sciencedirect, Google Scholar, and Web of Science) were used to gather information using several keywords that include one of the 4 terms i.e. *Pistacia lentiscus*, lentisk, mastic, and Chios mastic gum in combination with other terms: Oil, triterpenes, phenolics, flavonoids, fatty acids, variability, extraction, authentication, standardization, quality control, delivery system, and nano. The number of identified articles included 85 articles after excluding non-indexed journals and pure biological articles.

Pistacia lentiscus phytochemical composition

P. lentiscus extracts encompass various metabolites from different classes, such as volatile compounds, triterpenes, phenolic acids, flavonoids, fatty acids, phytosterols, and carotenoids (Fig. 1). The upcoming subsections provide an overview of *P. lentiscus* metabolites (volatile compounds, triterpenes and steroids, phenolics, lipid extracts' metabolites) in context to different extract (e.g. gum) and organ (e.g. leaf, fruit, etc.) types.

Volatile compounds

Volatile compounds, especially found in essential oils, of *P. lentiscus* are mostly represented by monoterpenes and sesquiterpenes, which are derived from the isoprenoid pathway. For plants, these compounds serve important roles such as attracting pollinators and repelling predators (Tetali 2019). For humans, due to their aroma and/or therapeutic activities (such as anti-inflammatory and antioxidant ones), essential oils find several culinary and health applications, and in cosmetics (Francomano et al. 2019; Tetali 2019; Wojtunik-Kulesza et al. 2019). Table 1 summarizes the percentage of different volatile compound classes in *P. lentiscus* extracts from various origins.

Gum (oleogum)

A study in turkey analyzed oil samples from 2 wild and 1 cultivated *P. lentiscus* grown in different areas. GC-FID and GC–MS revealed 48 volatiles with α-pinene

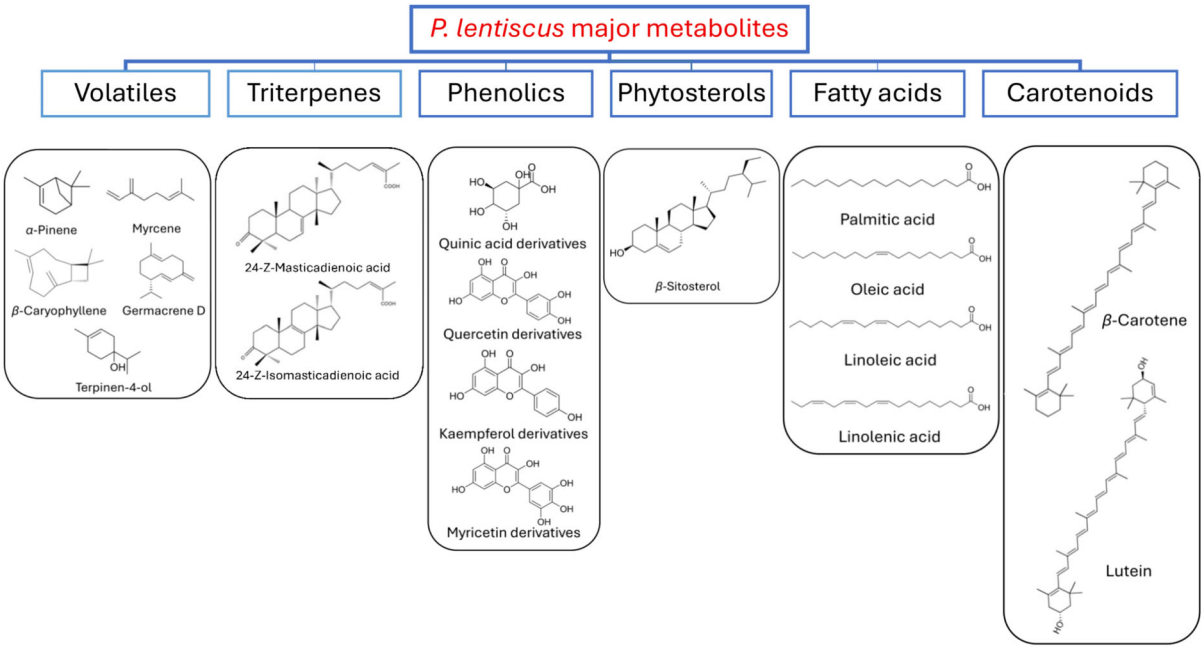


Fig. 1 An overview of *P. lentiscus* major metabolites from different chemical classes

Table 1 Major volatile compound classes (%) identified in *P. lentiscus* essential oils of gum and leaves from different geographical origins

Organ/Source	Origin of material	Major volatile compound classes				References
		Monoterpene hydrocarbons (%)	Oxygenated monoterpenes (%)	Sesquiterpene hydrocarbons (%)	Oxygenated sesquiterpenes (%)	
Gum essential oils of wild trees	Turkey	**76.9–81**	6	5.9–8	3.1–5.4	Tabanca et al. (2020)
Gum essential oil of cultivated tree		**85**	5.8	4.9	1.2	
Leaf	Egypt	**75.57**	1.16	12.17	1.5	El Bishbishy et al. (2020)
Leaves from different areas	Spain	**35.8–74.9**	0.2–22.5	12.3–43.9	With diterpenes reached from 0.8 to 3.1	Llinares et al. (2021)
Leaf	Palestine	**87**	1.55	11.39	–	Jaradat et al. (2022)
Leaves from different sites	Algeria	5–42	3–9	**29–46**	13–37	Sehaki et al. (2022)
Leaf	Morocco	2.31	9.95	35.87	**45.07**	Drioiche et al. (2023)

(52 and 56.2%) and myrcene (19 and 20%) dominating wild trees' oils, while cultivated tree's oil was characterized by α-pinene (71%) and lower levels of β-pinene (6%) and myrcene (3%). Results revealed that factors such as cultivation method, trees' age, soil type, and bioclimatic conditions influenced aroma

composition (Tabanca et al. 2020). Furthermore, α-pinene and β-myrcene were identified as the main components in commercial mastic gum and mastic oil in Chios. α-Pinene accounted for 74.61% in gum and 83.15% in oil samples, while β-myrcene represented 7.01% and 5.14%, respectively. Notably, GC–MS provided more detailed results unique to the gum sample, revealing additional high-boiling volatiles, namely farnesol (1.3%) and 3-pentadecylphenol (3.4%) (D'Auria and Racioppi 2022). These findings suggest expanding applications for gum components in healthcare and industrial fields, such as incorporation of farnesol in topical solutions for psoriasis, and formation of copolymers with anisotropic proton conduction using 3-pentadecylphenol (Cieslik-Boczula et al. 2009; Delmondes et al. 2020; Lapczynski et al. 2008).

Leaf and fruit

GC-FID and GC–MS were employed to assess essential oil composition derived from leaves and twigs belonging to 5 different sites in Spain. The study revealed various terpenes classes as follows: Monoterpene hydrocarbons (35.8–74.9%), sesquiterpene hydrocarbons (12.3–43.9%), and oxygenated monoterpenes (0.2–22.5%). α-Pinene (2.8–39.2%), myrcene (0.6–59.3%), β-phellandrene (0.0–42.8%), germacrene D (3.9–20.4%), terpinen-4-ol (0.2–19.0%), β-caryophyllene (3.4–17.1%), β-pinene (0.3–17.1%), and δ-3-carene (0.2–15.7%) were the major forms (Llinares et al. 2021). Likewise, Egyptian samples were characterized by monoterpene hydrocarbons (75.57%) predominated with α-pinene (38.14%), D-limonene (11.9%), α-phellandrene (10%), and β-pinene (9.5%) (El Bishbishy et al. 2020). Moreover, an oil sample from Palestine, which shares a close geographical origin to Egypt, showed enrichment in monoterpene hydrocarbons (87.06%) with limonene (43.78%), α-pinene (29.45%), and β-pinene (7.54%) as major forms (Jaradat et al. 2022).

On the other hand, leaf oil samples from the mountainous and littoral sites in Algeria revealed sesquiterpene hydrocarbons (29–46%) as the abundant class, followed by monoterpene hydrocarbons (5–42%), with β-caryophellene (8–25%), δ-cadinene (3–8%), β-myrcene (0.1–19%) and α-pinene (2–13%) as major volatiles (Sehaki et al. 2022). Another leaf sample from Morocco showed an even stronger dominance of oxygenated sesquiterpenes (45.07%) followed by sesquiterpene hydrocarbons (35.87%). Spathulenol (18.57%) and germacrene D (17.54%) predominated in this sample (Drioiche et al. 2023). Such findings emphasize the region's unique environmental factors impacting essential oil profiles.

In another study, cineol (29.17%) and α-pinene (25.2%) predominated a leaf oil sample from Morocco (Hayani et al. 2024). The presence of cineol was further confiremed by the detection of cineol derivatives in other leaf extracts (Anagnostou et al. 2023; Stefi et al. 2021). Besides, Djebari et al. further investigated the leaf and fruit methanol extracts from Algeria using GC–MS and SPME–GC–MS. The results revealed 44 compounds (33 in leaf and 23 in fruit extracts) classified as phenols/polyphenols, monoterpenes/sesquiterpenes, alkanes, dienes, alcohols, ketones, carboxylic acids, esters, aromatics, benzofurans, heterocyclics, and monoglycerides (Djebari et al. 2021), suggestive for future pharmacological and toxicological studies to evaluate these compounds activities.

Collectively, these studies demonstrate that *P. lentiscus* essential oils exhibit chemo-diversity according to different plant extracts, cultivation status, and environmental factors across the Mediterranean basin. While monoterpene hydrocarbons, i.e., α-pinene and myrcene, dominate gum and gum oils from Greece and Turkey, leaf profiles shift between monoterpene-rich chemotypes in Spain as well as Eastern Mediterranean regions (e.g., Egypt and Palestine) and sesquiterpene-enriched profiles in North-West Africa (e.g., Algeria and Morocco).

Triterpenes and steroids

Triterpenes are another group of secondary metabolites derived from isoprenoid pathway (Mantiniotou et al. 2025) in either tetracyclic, such as dammarane, tirucallane, and apotirucallane derivatives, or pentacyclic, such as oleananes, ursanes, and lupanes (Mantiniotou et al. 2025; Noushahi et al. 2022). They exhibit therapeutic activities against several disorders, i.e., cardiovascular diseases and diabetes (Ghiulai et al. 2020; Nazaruk and Borzym-Kluczyk 2015; Peng et al. 2024), and show diverse composition in different plant extracts as explained in the next subsections.

Gum

Triterpenes represent the major class in gum, accounting for *ca.* 65–70% of the gum total weight and are represented mainly by tetracyclic and pentacyclic triterpenes. CMG triterpenes are subdivided into 2 fractions: acidic and neutral. Acidic fraction mainly contains 4 dammaranes, namely 24-*Z*-masticadienonic acid (MNA), 24-*Z*-isomasticadienonic acid (IMNA), 24-*Z*-masticadienolic acid as well as 24-*Z*-isomasticadienolic acid, and 3 oleananes, namely oleanonic acid, moronic acid, and 18-α-H-oleanonic acid. In contrast, the neutral fraction includes chiefly tirucallol, dammaradienone, 28-norolean-12-en-3-one, oleanonic aldehyde, and oleanolic aldehyde (Ottria et al. 2023).

Recent studies reported on new triterpenoids belonging to different derivatives, including bicyclic polypodane, tirucallane, apo-tirucallane, nor-dammarane, oleanane, nor-oleanane, and masterpenoids isolated from commercial mastic gum sold in China (An et al. 2024a, b, 2022; Liu et al. 2021, 2022; Xiang et al. 2025; Yu et al. 2022), which have yet to be tested for biological effects determination. Likewise, UHPLC-Q-Orbitrap-HRMS revealed A-seco-tirucallane-type terpenic acids for the first time in mastic samples, which were sold in China (Kahaer et al. 2024), underscoring the efficacy of this technique in analyzing complex resin samples.

Leaf and stem

Lupeol, a common triterpene, was isolated from the ethyl acetate fraction of the distilled leaf' methanol extract (Elloumi et al. 2022a). An Anti-herpes simplex virus type 2 (HSV-2)-guided assay led to the isolation of two triterpenoids, dammaradienone and dammaradienol, from the methanol extract of Tunisian *P. lentiscus* stems (Bouslama et al. 2020). Besides neutral and acidic triterpenes, which are already common in gum, phytosterols (1428.4 µg/g dry weight (DW); sitosterol (1356.62 µg/g DW), campesterol, and stigmasterol) and steroid ketones (164.23 µg/g DW; sitostenone (126.75 µg/g DW) and tremulone) were detected in a diethyl ether extract of leaves from Algeria (Gadouche et al. 2023), warranting for comparative bioassays between gum and leaves. In addition, other steroids were detected in leaf and fruit lipid extracts as we discussed in "Lipid extracts' metabolites". subsection.

Generally, gum extracts are rich in triterpenes, whereas leaf extracts contain both triterpenes and steroids.

Phenolics

Phenolics, found ubiquitously in *planta*, are divided according to their skeletons into subclasses including phenolic acids, flavonoids, coumarins, tannins, lignans, and stilbenes (Sun and Shahrajabian 2023). They play a major role in improving plant fitness against various abiotic and biotic stressors (Jan et al. 2021). For instance, flavonoids protect plants from ultraviolet (UV) light (Ferreyra et al. 2021). They also exhibit biological effects in humans, i.e., antioxidant, anti-inflammatory, antimicrobial, anticancer, neuroprotective, wound healing, and skin health promotion activities (Sun and Shahrajabian 2023). Table 2 highlights the available literature data enabling quantitative comparison of phenolic compounds across different *P. lentiscus* extracts.

Gum

Unlike essential oils and triterpenes, only two studies, in almost 20 years, investigated the phenolic fraction of the gum. The first study quantified tyrosol (375 ng/g resin), *p*-hydroxybenzoic (136 ng/g resin), *p*-hydroxyphenylacetic (107 ng/g resin), and vanillic (41 ng/g resin) in a gum methanol extract from Chios (Kaliora et al. 2004). In the another study, *P. lentiscus* gum acetone, ethanol, and methanol extracts derived from trees of different ages in Turkey displayed 22 phenolics represented by rosmarinic (25.14–456.30 mg/kg extract), salicylic (66.06–143.56 mg/kg), and caffeic (6.66–99.64 mg/kg) acids as major ones (Sarikahya et al. 2024), suggestive for predominance of phenolic acids in gum extracts. Notably, tyrosol and rosmarinic acid contents are far below tyrosol in olive oil (1.4–10.8 µg/g oil) (Lopez-Bascon et al. 2024) and rosmarinic acid in rosemary (12–32 mg/g) (Bejenaru et al. 2024), indicating that *P. lentiscus* resin is not among the primary sources for these metabolites.

Leaf In contrast to gum enriched in terpenes, *P. lentiscus* leaves represent a richer source for different phenolic classes. Extracts of different polarities

Table 2 Comparative profiles of major phenolics detected in *P. lentiscus* gum, leaf, and fruit extracts

Class	Origin			
	Turkey (Sarikahya et al. 2024)		Croatia (Elez Garofulic et al. 2020)	
	Type of extract			
	Acetone, ethanol, and methanol extracts from trees of different ages (mg/kg extract)		Methanol extracts (mg/100 g)	
	Organ/Source			
	Gum	Leaf	Leaf	Fruit
Phenolic acids	Rosmarinic acid (25.14–456.30), Salicylic acid (66.06–143.56), Caffeic acid (6.66–99.64), Ellagic acid (5.94–14.65), Chlorogenic acid (0.24–4.23)	Rosmarinic acid (23.64-327.75), Salicylic acid (57.55–439.85), Ellagic acid (33.15–325.18), Caffeic acid (18.87–138.48), Dihydro caffeic acid (17.96–35.20), Chlorogenic acid (0.30–14.81)	Gallic acid (4.34), 5-*O*-Galloylquinic acid (3.08), Feruloylquinic acid (2.29), Chlorogenic acid (0.27)	Gallic acid (59.27), 5-*O*-Galloylquinic acid (0.6), Feruloylquinic acid (1.38), *p*-Coumaric acid (0.89), Chlorogenic acid (0.22)
Flavonols	Rutin (1.76–12.69), Quercetin (0.31–3.26)	Quercetin (9.87–709.01), Quercitrin (27.00–850.81), Myricetin (6.71–75.02), Rutin (14.92–192.55)	Myricetin (304.09), Myricetin rhamnoside (1782.39), Myricetin glucuronide (750), Myricetin rutinoside (528.9), Quercetin rhamnoside (130.92), Quercetin-3-glucoside (39.33), Quercetin-3-hexoside (31.94), Quercetin pentoside (10.64), Kaempferol-3-hexoside (19.44), Kaempferol rhamnoside (11.29), Kaempferol rhamnosyl hexoside (2.44), Kaempferol-3-rutinoside (2.41), Kaempferol pentoside (2.13)	Myricetin (14.64), Myricetin glucuronide (251.44), Myricetin rutinoside (172.63), Myricetin rhamnoside (24.72), Quercetin-3-glucoside (156.61), Quercetin-3-hexoside (23.94), Quercetin rhamnoside (1.9), Quercetin pentoside (1.07), Kaempferol rhamnoside (2.17), Kaempferol rhamnosyl hexoside (1.91), Kaempferol-3-rutinoside (1.93), Kaempferol-3-hexoside (1.75), Kaempferol pentoside (1.60)
Flavanols	(-)-Epigallocatechin (2.14–17.61)	()-Epigallocatechin (244.13–1483.28), ()-Epigallocatechin gallate (6.35–728.50), ()-Epicatechin (10.43–148.16), ()-Epicatechin gallate (9.23–143.53)	Catechin (31.70), Epicatechin (31.66), Epigallocatechin gallate (9.16), Epicatechin gallate (1.47), Procyanidin B1 (13.58), Procyanidin B2 (10.72)	Catechin (18.56), Epicatechin (18.28), Epigallocatechin gallate (1.76), Epicatechin gallate (1.26), Procyanidin B1 (20.69), Procyanidin B2 (11.93)

Table 2 continued

Class	Origin			
	Turkey (Sarikahya et al. 2024)		Croatia (Elez Garofulic et al. 2020)	
	Type of extract			
	Acetone, ethanol, and methanol extracts from trees of different ages (mg/kg extract)		Methanol extracts (mg/100 g)	
	Organ/Source			
	Gum	Leaf	Leaf	Fruit
Flavones	Scutellarein (3.79–29.80), Luteolin (3.41–23.51), Apigenin (1.08–5.90), Chrysoeriol (1.83–4.43), Hispidulin (0.60–4.52), Acacetin (0.51–2.03), Chrysin (0.30–0.65), Luteolin-7-glucoside (0.89–27.44), Apigenin-7-glucoside (0.51–5.51)	Scutellarein (32.76–1361.19), Luteolin (28.18–1327.26), Apigenin (6.24–345.78), Chrysoeriol (3.32–17.60), Hispidulin (1.66–41.40), Acacetin (0.71–8.20), Chrysin (0.38–7.20), Luteolin-7-glucoside (5.84–75), Apigenin-7-glucoside (1.26–50.52)	Luteolin (26.54), Apigenin (2.02)	Luteolin (1.54), Apigenin (0.15)
Flavanones	Naringenin (1.75–20)	Naringenin (6.76–66)	–	–
Flavanonols	(+)-Trans taxifolin (0.08–1.50), Dihydrokaempferol (0.08–0.48)	(+)-Trans taxifolin (4.89–250.18), Dihydrokaempferol (1.11–34.69)	–	–
Tannins	–	–	Digalloylquinic acid (605.88), Trigalloylquinic acid (102.1), Monogalloyl glucose (18.76)	Digalloylquinic acid (57.39), Trigalloylquinic acid (13.59), Monogalloyl glucose (15.08)
Others	–	Sclareol (4.89–884.74), Pyrogallol (15.39–46.60)	–	–

obtained from *P. lentiscus* trees of different ages in Turkey, i.e., acetone, ethanol, and methanol, showed higher number of compounds (31) in comparison with gum (22). Flavonoids were the most abundant class with scutellarein (32.76–1361.19 mg/kg extract) and quercetin (9.87–1277.84 mg/kg) as major ones (Sarikahya et al. 2024). Another methanol extract of leaves from Morocco revealed catechin as the predominant phenolic (37.045%) followed by 4-hydroxybenzoic acid (17.763%), coumaric acid

(17.589%), naringin (8.914%), *p*-coumaric acid (7.107%), quercetin (6.739%), and luteolin (4.839%) (Ouahabi et al. 2023).

Furthermore, Stefi et al. assessed methanol and aqueous fractions of *P. lentiscus* leaves (cultivated in the Athens Metropolitan area and native to Chios). The analysis identified 15 compounds belonging to galloyl derivatives of quinic acid, and flavonoids (Stefi et al. 2021). The presence of galloyl derivatives of quinic acid was further confirmed in the aqueous fraction of *P. lentiscus* leaves from Chios (Anagnostou et al. 2023). Other studies detected galloyl derivatives of quinic acid in aqueous and butanol fractions of Algerian leaves (Boucheffa et al. 2022), in an aqueous decoction from Morrocco (Drioiche et al. 2023), and other leaf extracts from Tunisia, Croatia, and Egypt (Dragovic et al. 2020; El Bishbishy et al. 2020; Elez Garofulic et al. 2020; Kayel et al. 2024), suggestive for their polar nature being enriched in butanol and aqueous extracts. Furthermore, Dragovic et al. quantified 5-*O*-galloylquinic; 3,5-di-*O*-galloylquinic; 3,4,5-tri-*O*-galloylquinic acids at 53.7–186.5, 16.4–95.5, and 10.6–57.5 mg/L, respectively in leaf methanol extracts from different areas in Croatia (Dragovic et al. 2020). Several studies reported antioxidant, antifungal, and gastroprotective activities for galloyl quinic acid derivatives (Baratto et al. 2003; Motta et al. 2017; Sannomiya et al. 2022).

Another study in Croatia demonstrated the predominance of myricetin and quercetin glycosides in leaf alcoholic extracts. Myricetin-3-*O*-rhamnoside was the most abundant flavonol glycoside (17.4 to 97.5 mg/L) followed by myricetin-3-*O*-glucoside (8.12 to 57.4 mg/L), myricetin-3-*O*-glucuronide (2.6 to 26.6 mg/L), and quercetin-3-*O*-rhamnoside (3.6 to 23.6 mg/L) (Dragovic et al. 2020). Other studies in Tunisia explored the ethyl acetate fraction of distilled leaf methanol extract detecting flavonol glycosides of myricetin, quercetin, and kaempferol. Myricetin-3-*O*-rhamnoside, quercetin-3-*O*-rhamnoside, and kaempferol-3-*O*-rhamnoside were detected at 12.17, 10.47, and 4.53 mg/g DW, respectively (Elloumi et al. 2022a, b). Other studies in Chios, Egypt, Algeria, Morocco, and Tunisia confirmed the presence of myricetin, quercetin, and kaempferol glycosides (Anagnostou et al. 2023; Boucheffa et al. 2022; El Bishbishy et al. 2020; Kayel et al. 2024; Seddoqi et al. 2024), presenting *P. lentiscus* leaves (even distilled ones) as a valuable source of various flavonol glycosides, especially myricetin and quercetin ones, which hold diverse biological activities, such as antioxidant and anti-inflammatory effects (Hayder et al. 2008; Nascimento et al. 2017; Yang et al. 2018).

Fruit

Stem, bark, and root Unlike leaf, fewer studies assessed the phenolic profile of fruit. For example, a study identified 30 phenolics belonging to phenolic acids (2–49 mg/100 g DW), flavonoids (142.8–379 mg/100 g DW), and anthocyanins (4.4–1373 mg/100 g DW) in methanol extracts from Algeria (Aissat et al. 2022), revealing fruits as a source of the latter class, which possess antioxidant, anti-inflammatory, antiviral, and anticancer activities (Bhaswant et al. 2023). Interestingly, protocatechuic acid (49–39 mg/100 g DW at unripe fruits) and a stilbene derivative called *trans*-piceid (Maximum 0.22 mg/100 g DW at red unripe fruits) were detected for the first time in *P. lentiscus* fruit, though devoid of kaempferol derivatives (Aissat et al. 2022). This is in accordance with a study in Croatia reporting ~ 654 mg/100 g flavonols in fruit methanol extract (with only 7.7 mg/100 g kaempferol derivatives) in comparison with ~ 3300 mg/100 g flavonols in leaf extract (Elez Garofulic et al. 2020), confirming that *P. lentiscus* leaves is a valuable source for flavonols. Protocatechuic acid is known for a variety of pharmacological activities, including antioxidant, anti-inflammatory, neuroprotective, antibacterial, antiviral, antiaging, anticancer as well as kidney and liver protective activities (Song et al. 2020). Phenolic compounds were also detected in fruit and seed fatty oils as we highlighted in ("Lipid extracts' metabolites" subsection).

Concerning *P. lentiscus* other organs, a study in Saudi Arabia demonstrated that leaf methanol extract was enriched in phenolics (28.4 mg gallic acid equivalent (GAE)/g) than stem (2.96 mg GAE/g) and root (2.62 mg GAE/g) extracts. 3,5-*O*-Digalloylquinic acid predominated in these organs' extracts, suggestive for an ecological role for galloylquinic acid derivatives in this plant (Al-Zaben et al. 2023). Another study in Egypt reported several flavonols in bark methanol extract, such as quercetin, quercetin-3-*O*-*β*-glucoside, kaempferol, kaempferol-3-*O*-*α*-rhamnoside, and kaempferol-3-*O*-*β*-glucoside (Selim et al. 2022), to be quantified in future studies.

Overall, *P. lentiscus* gum is particularly rich in phenolic acids, whereas leaf extracts encompass a broader diversity of phenolic compounds besides phenolic acids, notably galloylquinic acid derivatives and glycosides of myricetin and quercetin. Fruits represent an important source of anthocyanin pigments.

Lipid extracts' metabolites

Lipid extracts of *P. lentiscus* leaf and fruit encompass fatty acids, phytosterols (especially β-sitosterol), tocopherols (mainly α-tocopherol), and carotenoids. Concerning fatty acids, *P. lentiscus* oil composition is rich in palmitic, oleic, linoleic and/or linolenic acids, with higher levels of unsaturated fatty acids (UFAs) than saturated ones, imparting a biological activity and nutritional value for *P. lentiscus* oil (Nagy et al. 2024). This is due to oleic acid's anti-inflammatory activities (Santa-María et al. 2023) as well as linoleic and linolenic acids cardioprotective and antidiabetic actions (Jackson et al. 2024; Rajaram 2014) that counteract the unhealthy outcomes of palmitic acid (Mancini et al. 2015). In addition, β-sitosterol, α-tocopherol (vitamin E), and carotenoids exhibit several biological activities, i.e., antioxidant, anti-inflammatory, antidiabetic, anticancer, anti-obesity, and cardioprotective activities (Bhaswant et al. 2023; Crupi et al. 2023; Khan et al. 2022; Shahidi and de Camargo 2016). Table 3 summarizes the percentage of fatty acid classes, whereas Table 4 highlights the composition of tocopherols, sterols, and carotenoids in *P. lentiscus* leaf and fruit lipid extracts.

Leaf

The GC–MS analysis of lipid extracts from Algeria revealed the prevalence of polyunsaturated fatty acids (PUFAs) (27–55%), followed by saturated fatty acids (SFAs) (34–39%), and finally monounsaturated fatty acids (MUFAs) (3–31%). Linolenic acid displayed the highest levels (17 to 35%) followed by palmitic acid (24 to 31%), linoleic acid (9 to 28%), and oleic acid (2 to 30%), depending on the site of collection (Sehaki et al. 2022). Other studies in Algeria confirmed the predominance of PUFAs > SFAs > MUFAs with α-linolenic, linoleic, palmitic, myristic, and oleic acids as major forms (Harrat et al. 2018, 2020). Following the same methodology, Ouahabi et al. confirmed the prevalence of USFs, with linoleic (40.97%), oleic (23.69%), and palmitic (22.83%) acids as major fatty acids in samples from Morocco (Ouahabi et al. 2023). Accordingly, lipid extracts obtained from leaves require proper storage because PUFAs are more labile for oxidation to harmful products (Nagy et al. 2024; Saini et al. 2021). Also, studies have highlighted the anti-inflammatory and immunomodulatory activities of ω-3 fatty acids, including linolenic acid (Juric et al. 2022; Ren and Chung 2007).

Besides fatty acids, HPLC revealed α-tocopherol as the major tocopherol followed by δ- and β-tocopherols, while γ-tocopherol was absent in samples from Algeria (Harrat et al. 2018, 2020), suggestive for amending *P. lentiscus* leaf lipid extracts with other ones contain γ-tocopherol to provide full spectrum of tocopherols.

Fruit and seed In contrast to leaf lipid extracts, several studies in North Africa i.e., Tunisia, Algeria, and Morocco, demonstrated that MUFAs predominated in fruit and seed fatty oils, followed by similar levels of SFAs and PUFAs, which deviates from the PUFAs > SFAs > MUFAs accumulation pattern observed in leaf lipids. Oleic, palmitic, and linoleic acids were identified as major forms (Ait Mohand et al. 2020; Belyagoubi-Benhammou et al. 2018; Ben Ameur et al. 2024; Charef et al. 2008; Dhouibi et al. 2020; Ghzaiel et al. 2021; Mezni et al. 2014a; Trabelsi et al. 2012). This is in accordance with another study in Italy reporting the prevalence of MUFAs (46%) followed by PUFAs and SFAs (25%), with oleic (44%), linoleic (24%), and palmitic (23%) acids showing maximum levels (Siano et al. 2020). The prevalence of MUFAs makes fruit fatty oils more resistant to oxidation (Abrante-Pascual et al. 2024). Additionally, due to enrichment of MUFAs in *P. lentiscus* fruit oil, it can provide numerous health benefits, including weight loss and reducing the risk of inflammation, insulin resistance, cardiovascular diseases, and cancer (Kim et al. 2023).

Furthermore, several studies reported phytosterols, carotenoids, and tocopherols in fruit oils. GC analysis revealed β-sitosterol as the major sterol at 705 to 750 mg/kg oil in Italian berry oil samples collected over 4 years (Siano et al. 2020). Another study in Tunisia also demonstrated the predominance of β-sitosterol at 854.12 to 1224.09 mg/kg of oil in samples obtained from different sites (Mezni et al. 2016),

Table 3 Fatty acid classes (%) in *P. lentiscus* lipid extracts of leaves and fruits from different geographical origins

Organ and extract type	Origin of material	Fatty acid classes			References
		PUFAs (%)	MUFAs (%)	SFAs (%)	
Leaf petroleum ether extracts collected from different areas	Algeria	**40.56–65.27**	3.66–9.98	21.96–38.58	Harrat et al. (2018)
Leaf petroleum ether extracts collected during different seasons	Algeria	**18.54–65.27**	3.66–20.32	21.96–45.57	Harrat et al. (2020)
Leaf methanol–chloroform extracts from different sites	Algeria	**27–55**	3–31	34–39	Sehaki et al. (2022)
Leaf *n*-hexane extract	Morocco	UFAs (64.67%)		30.5	Ouahabi et al. (2023)
Fruit (red and black) fatty oils	Algeria	UFAs (78.8% in black – 83% in red)		(17% in red - 21.2% in black)	Charef et al. (2008)
Fruit fatty oil	Algeria	18	**52**	26	Belyagoubi-Benhammou et al. (2018)
Fruit fatty oils from different areas	Tunisia	~ 24.85	**44.43–53.08**	~ 25.74	Trabelsi et al. (2012)
Fruit fatty oils from different areas	Tunisia	UFAs (68.62–75.3%)		23.75–30.73	Mezni et al. (2014a)
Fruit and seed fatty oil	Tunisia	22.24	**48.62**	29.14	Dhouibi et al. (2020)
Seed fatty oil	Tunisia	17.85	**53.67**	28.77	Ghzaiel et al. (2021)
Fruit fatty oil	Tunisia	23.13	**42.73**	33.99	Ben Ameur et al. (2024)
Seed fatty oil from different localities	Morocco	~ 23.7	~ **53**	~ 23.28	Ait Mohand et al. (2020)
Berry fatty oil (samples collected over 4 years)	Italy	~ 25.7	~ **46**	~ 24.6	Siano et al. (2020)

suggestive for the superiority of the Tunisian oil as a source of β-sitosterol. Likewise, other studies in Tunisia confirmed the β-sitosterol predominance in *P. lentiscus* oil (Dhouibi et al. 2020; Ghzaiel et al. 2021; Trabelsi et al. 2012). HPLC analysis detected three carotenoids, namely lutein (1.74 to 4.62 mg/kg oil), zeaxanthin (0.47 to 1.93), and β-carotene (2.58 to 4.9) as well as two tocopherols identified as α-tocopherol (44.76 to 96.77 mg/kg oil) and γ-tocopherol (14.56 to 22.12) in fatty oil samples from Tunisian fruits (Mezni et al. 2014a). β-Carotene was the major form (7.22 mg kg^{-1} oil) (Ben Ameur et al. 2024)—vs. 70 mg/kg fresh carrot as one of the primary sources of β-carotene (Koca Bozalan and Karadeniz 2011)—in another fruit oil sample from Tunisia, alongside α-tocopherol (957.88 mg/kg), β-tocopherol (226.34 mg/kg), and γ-tocopherol (64.94 mg/kg) (Ben Ameur et al. 2024). Such enrichment of pro vitamin A and E pose fruit oil as potential antioxidant.

4-Monomethylsterols (obtusifoliol and citrostadienol at ~ 1.12 and ~ 1.88 mg/100 g oil, respectively) and 4,4-dimethylsterols (cycloartenol, 24-methylene cycloartenol, and butyrospermol recorded ~ 37.19, ~ 10.71, and ~ 1.31 mg/100 g oil, respectively) are intermediates in steroidal drugs manufacturing that were identified in oil samples from Tunisia *via* GC–MS (Trabelsi et al. 2016, 2012). Policosanol are fatty alcohols that were also detected in Tunisian samples (Trabelsi et al. 2016, 2015), suggesting potential lipid-lowering activity for Tunisian *P. lentiscus* oil due to policosanol's lipid- profile-improving effect (Gouni-Berthold and Berthold 2002).

To characterize the polar fraction of berry oil, UHPLC-ESI–MS/MS and HPLC–DAD identified 21 compounds belonging to phenolic acids, including *p*-hydroxybenzoic (~ 31.6 mg/kg oil), vanillic (~ 12.8), and gallic (~ 10.6) acids, as well as flavonoids, including quercetin 3-*O*-glucoside (~ 20.2 mg/kg oil) and eryodictiol (~ 13.6), in an oil sample from Italy (Siano et al. 2020). Another study reported protocatechuic acid and coumarin *via* HPLC–UV (at 0.140 and 0.650 mg Equivalent Quercetin/100 g oil, respectively) in a Tunisian seed oil sample (Ghzaiel et al.

Table 4 Composition and quantitative levels of tocopherols, sterols, and carotenoids in *P. lentiscus* leaf and fruit lipid extracts from different geographical origins

Organ and extract type	Origin of material	Chemical class			References
		Tocopherols	Sterols	Carotenoids	
Leaf petroleum ether extracts collected from different areas	Algeria	-(3.2–4.6 mg/g lipid) - α-Tocopherol (58.51–89.17% of total identified tocopherols), δ-tocopherol (7.59–27.47%), β-tocopherol (3.24–14.02%)	143.37–175.61 mg/g lipid	–	Harrat et al., (2018)
Leaf petroleum ether extracts collected during different seasons	Algeria	-(1.75–9.49 mg/g lipid) -α-Tocopherol (30.97 to 97.57% of total identified tocopherols), δ-tocopherol (2.43–65.17%), β-tocopherol (0–28.18%)	173.7–295 mg/g lipid	–	Harrat et al. (2020)
Fruit fatty oils from different areas	Tunisia	–	-(109.72–434.26 mg/100 g oil) -β–Sitosterol (~ 225.31 mg/100g oil), stigmasterol (~ 19.61), campesterol (~ 7.37), cholesterol (~ 4.46)	–	Trabelsi et al. (2012)
Fruit fatty oils from different areas	Tunisia	-(62.43–118.16 mg/kg oil) -α-Tocopherol (44.76–96.77 mg/kg oil), δ-tocopherol (14.56 –22.12)	–	-(5.8–10.57 mg/kg oil) β-Carotene (2.58 to 4.9 mg/kg oil), lutein (1.74–4.62), zeaxanthin (0.47–1.93)	Mezni et al. (2014a)
Fruit and seed fatty oil	Tunisia	–	β–Sitosterol (75.29%), campesterol (7.71%), Δ^5-avenasterol (4.91%), stigmasterol (4.49%)	–	Dhouibi et al. (2020)

Table 4 continued

Organ and extract type	Origin of material	Chemical class			References
		Tocopherols	Sterols	Carotenoids	
Seed fatty oil	Tunisia	α-Tocopherol (68.10 mg/kg oil)	-(154.89 mg/100 g oil) *β*–Sitosterol (67.25 mg/100 g), α-epoxysitostanol (33.36), 24-methylene cycloartenol (16.10), cycloartenol (9.35), campesterol (4.48), Δ^5-avenasterol (3.10), stigmasterol (2.69)	–	Ghzaiel et al. (2021)
Fruit fatty oil	Tunisia	-(1249.16 mg/kg oil) -α-Tocopherol (957.88 mg/kg oil), *β*-tocopherol (226.34), *δ*-tocopherol (64.94)	*β*-Sitosterol (80.19%), campesterol (5.20%), Δ^5-avenasterol (4.79%), stigmasterol (2.52%)	*β*-Carotene (identified as a major carotenoid at 7.22 mg/kg oil)	Ben Ameur et al. (2024)
Berry fatty oil (samples collected over 4 years)	Italy	–	*β*-Sitosterol (~ 728.5 mg/kg oil), squalene (~ 489.25), campesterol (~ 38.75), stigmasterol (~ 14.25)	–	Siano et al. (2020)

2021). Such phenolics boost oil stability against oxidation (Mikolajczak et al. 2021).

In summary, differences in chemical composition between *P. lentiscus* leaf and fruit lipid extracts make them suitable for different applications, such as protection against inflammation and cardiovascular diseases, respectively, with fruit oil is more stable against oxidation.

Miscellaneous compounds

Hydrosol is a byproduct of volatile oil production that consists of a small hydrophilic fraction that escapes into the distillation water steam. Santarsiero et al. employed ESI(+)-FT-ICR mass spectrometry to analyze the hydrosol sample resulting from Italian leaves' steam distillation. The study provided tentative chemical formulas prediction corresponding to 4 potential classes: terpenes, amino acids, peptides, and condensed heterocycles (Santarsiero et al. 2020). However, it must be noted that these assignments were based on accurate mass measurements without confirmation *via* tandem mass (MS/MS) fragmentation or chromatographic behavior; thus, the specific chemical identities are rather tentative. In solvent extracts, loliolide, a benzofuran derivative, was isolated from the ethyl acetate fraction of distilled leaf methanol extracts from Tunisia (Elloumi et al. 2022a; Maalej et al. 2021). Unlike the tentatively assigned hydrosol compounds, loliolide is a ubiquitous monoterpene lactone in the plant kingdom and has been previously investigated for its biological effects, including antioxidant, anti-inflammatory, antidiabetic,

anticancer, neuroprotective, antidepressant, and antiviral activities (Farzeen et al. 2025).

Differences in *P. lentiscus* metabolism

Environmental factors

The diversity of ecological (environmental) factors influences various aspects of plant life, including their metabolites' composition, especially secondary ones. Variation in factors such as temperature, humidity, and soil composition across different growing areas drives same plant populations to diversify their secondary metabolite profiles in response to available nutrients to cope with the surrounding conditions (Pant et al. 2021; Ramakrishna and Ravishankar 2011; Zandalinas et al. 2022).

Altitude variation is linked with alteration in other ecological factors. For example, as altitude increases, the average temperature decreases, while UV-B irradiation increases (Nataraj et al. 2022). Said and co-workers used GC–MS to investigate the effect of altitude on the terpenoid composition of *P. lentiscus* leaves collected from three regions of increasing altitude in Algeria. Statistical analysis revealed that monoterpene hydrocarbons increased with altitude elevation detected at 21.7, 37.5, and 221.5 µg/g DW as altitude increases. Principle component analysis (PCA) revealed that highlands and midlands were characterized by α-pinene (6.8%) and caryophyllene oxide (6.8%), respectively, in addition to *β*-caryophyllene and *δ*-cadinene in both groups (Said et al. 2011), which is in accordance with previous reports on a positive correlation between α-pinene and altitude (Aissi et al. 2016). Lowlands contained mainly *δ*-cadinene (10.9%), cubebol (10.5%), and *β*-bisabolene (7.7%) (Said et al. 2011), suggestive for *δ*-cadinene as possible marker for *P. lentiscus* essential oil being less influenced by altitude variability.

Another study addressed the effect of altitude on content of other metabolites in leaf methanol extracts from Morocco. Ascorbic acid (vitamin C) content increased significantly to reach 23.095 mg ascorbic acid equivalent/g dry matter (DM) at high altitude (1010 m) (Bendada et al. 2024) to protect *P. lentiscus* from UV radiation, offering extracts for skin-photoprotective formulations (Ravetti et al. 2019). Interestingly, total chlorophyll content showed a non-specific pattern with altitude (Bendada et al. 2024), suggestive for other ecological factors rather than altitude affecting chlorophyll biosynthesis. These results were further confirmed in another study on Moroccan leaves (Hadini et al. 2022).

To address the effect of soil type, a study assessed the effect of climate and soil composition on essential oil samples of leaves harvested from 5 different locations in Spain. α- and *β*-Pinene were found higher in sub-humid zones as well as fertile soils (characteristic by high cation exchange capacity and organic matter). In contrast, germacrene D and *β*-caryophyllene were positively correlated to high evapotranspiration index and calcaric arenosol soil, whereas, terpinen-4-ol was associated with drier climates and soils which are not calcareous or fertile (Llinares et al. 2021). In contrast, Aissi et al. reported higher levels of α-pinene and terpinen-4-ol in upper semi-arid bioclimate regions that are characterized by calcareous soils, while germacrene D elevated more in sub-humid and lower humid zones with clay-sandstone soils (Aissi et al. 2016), suggestive for more influence from other factors, such as altitude, rather than humidity and soil on terpenes profile or variability due to difference in study design.

Concerning phytosterols, Mezni and co-workers reported on the effect of growing region on sterol composition in Tunisian fruit fatty oil samples. PCA displayed cycloartenol (137 to 499 mg/kg oil), stigmasterol (31 to 79 mg/kg oil), and *β*-sitosterol (854 to 1224 mg/kg oil) as main discriminators between oils from various geographical origins (Mezni et al. 2016). Likewise, another study showed that tocopherols, carotenoids, and fatty acids levels of fruit fatty oil varied according to different growing areas in Tunisia (Mezni et al. 2014a).

Accordingly, the influence of environmental factors on *P. lentiscus* metabolite profiles is evident across both volatile and non-volatile constituents, reflecting adaptive responses to different ecological factors of various areas.

Seasonal variation and phenological stage

As typically observed *in planta,* seasonal variation is another source of secondary metabolites variability because it is linked with change in climatic conditions (Li and Zidorn 2022). Stefi and co-workers explored the seasonal variation effect on *P. lentiscus* L.

(cultivated in the Athens Metropolitan area and native to Chios) leaf samples collected in summer and winter. Quinic acid as well as monogalloyl derivatives of quinic and shikimic acids were higher in winter, while pistafolin A (gallotannin) and quinic acid digalloyl derivatives were elevated in summer (Stefi et al. 2021), suggestive for more complex metabolite biosynthesis in summer, and to be confirmed using genetic analysis. This was further confirmed by higher levels of tannins (phenolic polymers) in extracts of leaves collected during summer (Gori et al. 2020). Cineol glucosides were more concentrated in summer leaf extracts, and expected as resin is harvested at that time versus higher flavonoids' level *viz.* myricetin 3-*O*-xyloside, myricetin 3-*O*-rhamnoside, and luteolin in winter (Stefi et al. 2021).

Moreover, a study addressed the interaction between altitude and seasonal alteration as sources of variability in leaf essential oil samples from Algeria. Monoterpene hydrocarbons were higher at the mountains during all seasons except winter (28–42.8%) (Sehaki et al. 2022), which falls in accordance with previous reports concerning altitude (Aissi et al. 2016; Said et al. 2011). On the other hand, sesquiterpenes hydrocarbons, i.e., *β*-caryophyllene, showed highest levels at littoral sites, especially in summer (37.9–46.5%) (Sehaki et al. 2022), in accordance also with Aissi et al. (Aissi et al. 2016). Such results may indicate a protective role for essential oil components against stressors of summer.

Harrat and co-workers highlighted the effect of seasonal variation on fatty acids, tocopherols, and sterols content in leaves (Harrat et al. 2020), but the large variability of these classes composition passed the seasonal diversity, warranting future studies that use other approaches to study seasonal influences on metabolite profiles regardless of other factors. In this context, a study addressed the effect of altitude and seasonal variability on the lipid profile of leaf extracts from Algeria, revealing for oxylipids i.e., oleic, linoleic, and linolenic acids, as altitudinal and seasonal discriminators. Oleic acid was higher at low altitudes in summer (Sehaki et al. 2022), aligning with similar results about oleic acid content of soybean grown at high temperature (Ahmadi and Daneshian 2025), which may indicate a protective role for this acid in hot conditions due to its higher thermal stability than PUFAs. Linolenic acid was higher at the mountains in winter, and likewise observed to some extent in case of linoleic acid but at low altitude (Sehaki et al. 2022), confirming the role of PUFAs in maintaining cellular viability in cold climate (Mei et al. 2015).

Rather than climatic factors, variation in phenological (developmental) stage of plants also stands behind the effect of seasonal shifts on secondary metabolites production (Li and Zidorn 2022). This is likely attributed to development stages impact on the initiation and differentiation of plant organs cellular structures that produce and store secondary metabolites (Li et al. 2020). In this regard, a study observed that phenolic acid level maximizes in Croatian leaf samples at the flowering stage, suggesting a role for this class in flowers development, while flavonoids peak during the early fruiting stage (Dragovic et al. 2020). This aligns with another study on flavonols, particularly quercetin derivatives, constituted the majority of phenolics during unripe stages ranging from 58 to 61% of the total phenolic content in fruits from Algeria (Aissat et al. 2022), confirming the role of flavonoids in fruit development (Zheng et al. 2025). Anthocyanin pigments, mainly cyanidin and delphinidin conjugates, composed most of the phenolic content at ripe stages varying from 53 to 59% with delphinidins more predominant (Aissat et al. 2022), promoting the antioxidant activities of *P. lentiscus* fruits due to the additional OH of delphinidins (Sadowska-Bartosz and Bartosz 2024). Boudieb et al. confirmed the increase in total phenolic and anthocyanin contents during fruit maturation (Boudieb et al. 2019).

Developmental stage may also take part in fatty oil yield and composition variability (Ziyad et al. 2022). Boudieb and co-workers demonstrated that as fruit maturity progresses, the yield of fatty oil, and the number of its metabolites increase (Boudieb et al. 2019). Antioxidants such as squalene and α-tocopherol acetate (Keshari et al. 2022; Micera et al. 2020) were only present in black mature fruit oil (Boudieb et al. 2019). Likewise, other studies revealed same trend for oil yield with maturation (Charef et al. 2008; Mezni et al. 2014b; Mohand et al. 2022). On the other hand, another study reported a decrease in phenolics of fatty oil sample from Moroccan seeds with maturation (Mohand et al. 2022).

Bakhit and co-workers suggested harvesting of fruits at the initial ripening stage to obtain oil characterized by higher α- and *β*-tocopherols' content and, hence, greater antioxidant activity (Bakhti et al. 2024). Another study reported maximum levels of

cycloartenol as well as obtusifoliol and citrostadienol, sterol intermediates involved in steroidal drugs production, in fruit oil at 25th days and 75th and after fruiting, respectively (Trabelsi et al. 2016). Overall, such studies help in determining the optimum harvest time according to seasons and/or phenological stage to maximum the yield of various metabolites.

Plant organ type

Secondary metabolites also diversify according to the plant's various organs (Li et al. 2020). In this context, a study tracked the secretion ducts network along the *P. lentiscus* (cultivated in the Athens Metropolitan area) axis revealing variation in different organs exudates which may be due to ununified network of the secreting ducts or even if the network is unified, the preferential synthesis of certain metabolites in different organs may play a role in these observed variations (Stefi et al. 2021). Another study reported on the diversity of yield, total phenolic and flavonoid contents as well as chemical profile between leaf and stem methanol extracts from Morocco, with the highest yield in leaf (33% vs. 22% for stem). Catechin and myricetin were exclusive for leaf extract, whereas gentisic acid, hydroxytyrosol, and oleocanthal were only found in stem extract (Seddoqi et al. 2024), confirming the organ specific phytochemical profile observation of (Stefi et al. 2021). Future studies may be needed to confirm the presence of olive-related metabolites in other *P. lentiscus* extracts from different origins.

Furthermore, total phenolic and flavonoid contents were higher in leaves than stems (524.87 mg GAE/g DM and 147.91 mg Rutin equivalent (RE)/g DM vs. 85.27 mg GAE/g DM and 25.87 mg RE/g DM, respectively) (Seddoqi et al. 2024). Al-Zaben and coworkers confirmed this superiority, reporting highest phenolic content in a leaf methanol extract (28.4 mg GAE/g) versus stem (2.96 mg GAE/g) and root (2.62 mg GAE/g) extracts (Al-Zaben et al. 2023). Additionally, leaf methanol extract from Algeria encompassed 15 times higher phenolic and 20 times more flavonoid contents than fruit extract (Djebari et al. 2021), suggesting leaves as an efficient and economical source for phenolics from *P. lentiscus*.

Plant gender

Gender difference in dioecious plants is another source of variation that may stand behind the observed chemical variability. Generally, males allocate more resources for vegetative growth, while females push their resources toward sexual reproduction and defensive secondary metabolites production (Massei et al. 2006).

In case of *P. lentiscus*, a study in Tunisia evaluated the effect of the interaction between plant sex, plant organs (leaves, stems, flowers, and fruits), and phenological stages variability on essential oil profile and phenolic content. The oil yield was little affected by the factors examined, varying from 0.16% to 0.13%. Monoterpene hydrocarbons were higher in females, reaching a maximum level (94.1%) in unripe fruits. Sesquiterpene hydrocarbons were also superior in females reaching 73.2% in leaves of flowering stages (Yosr et al. 2018), suggesting a role for these volatiles in the sexual reproduction of *P. lentiscus* such as attracting pollinators (Qasim et al. 2024; Quarrell et al. 2023). On the other hand, oxygenated monoterpenes (7–18%) and oxygenated sesquiterpenes (16.0–51.6%) were higher in male organs (Yosr et al. 2018).

Concerning phenolics, they were higher in vegetative dormancy stage as manifested by male leaves aqueous acetone extracts showing higher phenolic content than females (106.5–209.1 in males vs. 87.0–178.5 GAE/g DW in females) for all growing stages. Flavonoid and tannin contents also elevated more in males for all tested organs with superiority for leaves (Yosr et al. 2018). These results orient industrial field to target female and male *P. lentiscus* as economical sources for volatile compounds and phenolics, respectively.

Effect of miscellaneous factors

Besides the aforementioned factors, which are summarized in Fig. 2, other factors such as cultivation method (cultivated or wild) and plant age play a role in chemical profiles diversity in different plant species (Li et al. 2020; Reyes-Goya et al. 2024). For example, a study on gum oil from wild and cultivated *P. lentiscus* in Turkey revealed that α-pinene (52 to 56.2%) and myrcene (*ca.* 20%) dominating wild oils, while cultivated oil was characteristic by α-pinene

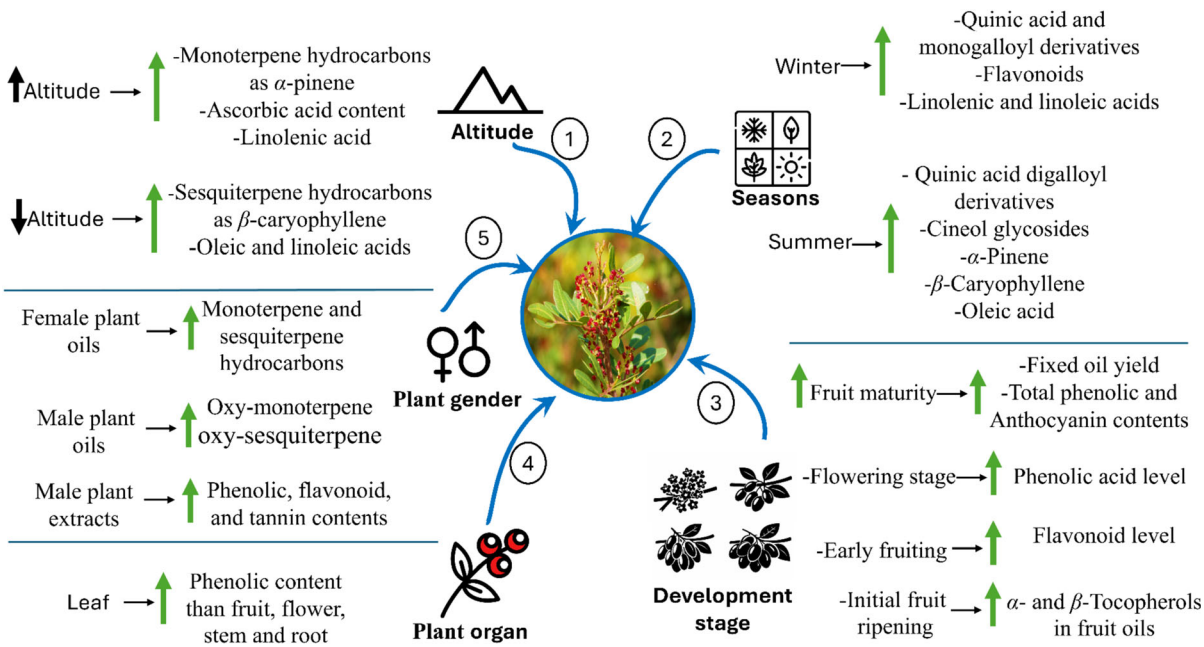


Fig. 2 Diagrammatic sketch illustrating factors affecting metabolites' composition of different *P. lentiscus* extracts

(71%) and lower quantities of *β*-pinene (6%) and myrcene (3%). The authors attributed this variability to several factors, including cultivation method and/or age of the trees (wild trees were about 100-year-old, whereas cultivated one was nearly 7-year-old) (Tabanca et al. 2020). In another study in Turkey, leaf hexane extracts from trees with various ages displayed palmitic acid among major acids in all ages except 100-year-old (17%). These 100-year-old trees were also characterized by the highest content of oleic acid (45.65%), suggesting this age for production of non-polar extracts with high biological quality (Sarikahya et al. 2024).

Application of fertilizers represents an approach in agriculture practice to enhance plants yield, quantitatively and quantitatively, as exemplified in *Pistacia vera* L. (pistachio) (Norozi et al. 2019). In this respect, a study investigated the effect of foliar $ZnSO_4$ on male tree of *P. lentiscus* in Turkey at concentrations (0, 0.2, 0.4, 0.8%) during 50% and 100% leafing stages for two consecutive years. Various Zn levels and leafing stages in both years did not significantly influence essential oil and α-tocopherol contents (Bayram et al. 2022), orienting future research to focus on other fertilizers common in *Pistacia* species agriculture practice.

Collection method of gum contributes to its chemical diversity, with difference in triterpenes composition between traditional method and liquid collection (characteristic by applying a stimulating agent on the incisions to enhance resin output). Traditional method was richer qualitatively with 36 triterpenes vs. 19 using liquid method. The main triterpenes were IMNA (24 and 22.5% w/w in the traditional and the liquid methods, respectively), MNA (9.3 and 14.7% w/w), and 28-norolean-17-en-3-one (19 and 36% w/w) (Assimopoulou and Papageorgiou 2005).

Aging of products due to storage is another factor that may be associated with alteration in quality and metabolomic composition of natural products (Zhu and Chen 2007). In this respect, a study reported the effect of aging on CMG samples. The essential oil yield decreased in the 2- and 10-year-old samples recording 3.5 mL/Kg or below, respectively (< the minimum content which is 10 mL/Kg dry resin according to the European Pharmacopeia). In comparison with fresh samples (stored for 2 or 6 months), monoterpene and sesquiterpene hydrocarbons decreased with simultaneous increase in oxygenated monoterpenes and sesquiterpenes, especially in 10-years aged samples (Pachi et al. 2021). Likewise, Paraschos et al. addressed the effect of gum aging over a shorter period (1:9 months) revealing an elevation in

α-pinene and a decline in β-myrcene levels (Paraschos et al. 2016), indicating alterations in biological activities of aged samples to be addressed in future studies to conclude the optimum storage period for gum to retain its biological activities.

Concerning methods of analysis, a study revealed α-pinene and β-myrcene as main components in commercial mastic oil and mastic gum sold in Chios via both GC–MS and HS–SPME–GC–MS, with more metabolites detected using latter technique. Interestingly, β-myrcene was more sensitive to HS–SPME–GC–MS, whilst α-pinene showed an opposite trend. The study attributed this behavior to SPME fiber preferential absorption of β-myrcene (D'Auria and Racioppi 2022), pointing out the influence analytical techniques variation on the results of chemical investigations. Finally, the adopted extraction solvent and extraction method play a role in the variability of plants extracts, both in yield and composition, as highlighted under the next section in this review ("Extraction and processing techniques" section).

In conclusion, addressing the diversity of *P. lentiscus* metabolites according to different factors paves the way for producing high-quality extracts suitable for different culinary and industrial purposes.

Extraction and processing techniques

Sample extraction plays a pivotal role in the application of natural extracts. Factors such as concentration and polarity of the extractant, pH, pressure, and temperature affect the desorption and solubilization of targeted phytocompounds; hence, extraction method efficiency (Gil-Martín et al. 2022). Accordingly, the upcoming subsections will discuss various extraction methods reported on *P. lentiscus* extracts, concluding the optimum conditions for maximum yield of different metabolites.

Solvent extraction (SE)

SE is a widely used technique for yielding bioactive fractions, including polyphenols and flavonoids, from plant materials (Alara et al. 2021). The efficiency of SE is influenced by several factors, including the drying state of the plant material, the type of solvent, and the specific plant tissues being extracted.

The drying state of the plant material is a key factor affecting the recovery of bioactive compounds. Fresh plant materials often facilitate better polar solvent penetration due to natural moisture content, as residual moisture enhances the swelling of plant tissues and the mass transfer of hydrophilic compounds. In contrast, for non-polar solvents, excessive moisture can act as a barrier, hindering the solvent's contact with the hydrophobic matrix and thus reducing extraction efficiency (Belwal et al. 2022). For *P. lentiscus*, studies comparing extraction yields suggest that fresh leaves may provide a higher recovery of phenolics compared with dried leaves, as the drying process can lead to the degradation of sensitive compounds (Bampouli et al. 2015).

The choice of solvent also critically influences extraction efficiency. Polar solvents, such as water and methanol, are generally more effective for extracting hydrophilic constituents compared to non-polar solvents. For instance, comparisons of *P. lentiscus* extracts prepared with solvents of varying polarity (water, methanol, and hexane) indicated that water and methanol resulted in significantly higher yields of phenolic fractions compared to hexane (Barbouchi et al. 2020). Such a pattern highlights the superior efficacy of polar solvents for isolating hydrophilic phytochemicals from this species.

The specific plant tissue utilized is another determinant of yield (Fig. 3). Literature comparing different tissues specifically of *P. lentiscus* indicates that leaves typically accumulate higher concentrations of phenolic compounds compared to fruits (Barbouchi et al. 2020; Saini et al. 2024). Overall, current literature suggests that the extraction of phenolic fractions from *P. lentiscus* is most efficient when using fresh leaves and polar solvents, such as water.

Ultrasonic-assisted extraction (UAE)

UAE is a rapid and efficient method that enhances solvent penetration and mass transfer, accelerating the extraction process by utilizing high-frequency sound waves to induce cavitations, allowing for the efficient release of bioactive compounds (Sharayei et al. 2021).

For example, the UAE process for extracting polyphenols from *P. lentiscus* fruits has been optimized using deep eutectic solvents (DES) composed of choline chloride and glycerol. The extraction efficiency was significantly influenced by factors such

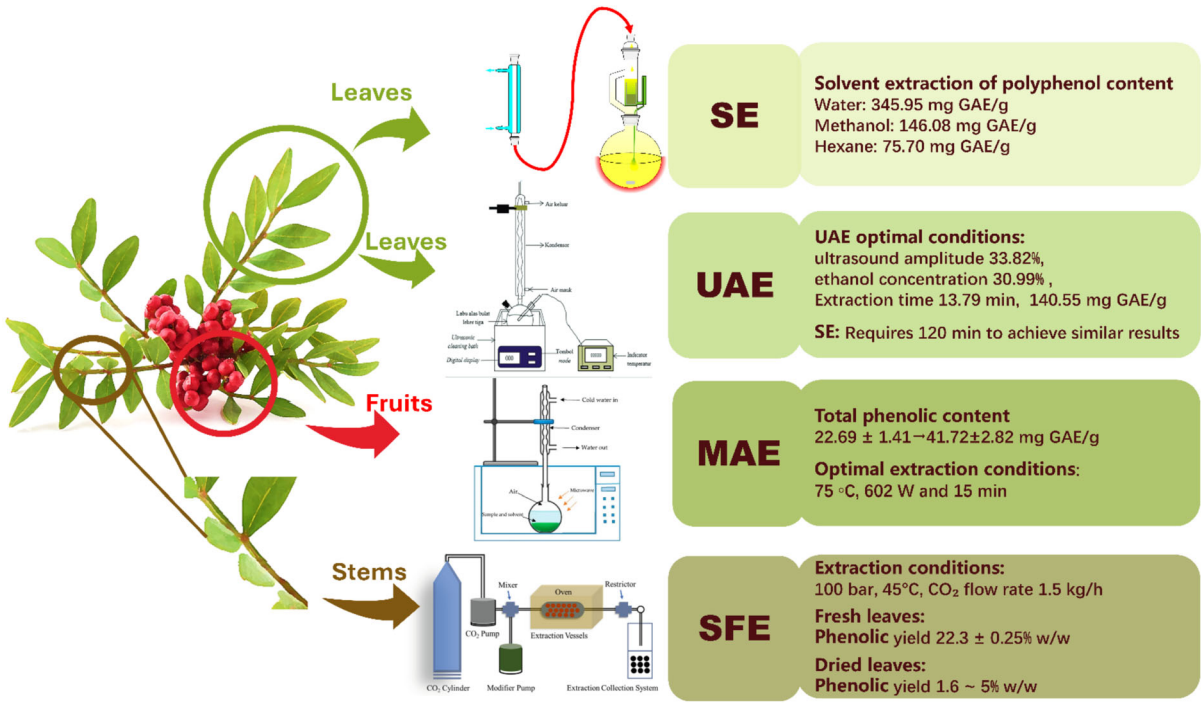


Fig. 3 Summary of optimum extraction conditions of SE, UAE, MAE, and SFE to prepare *P. lentiscus* different extracts

as the DES/water ratio, temperature, and extraction time. Under optimal conditions—28.3% water content, 40°C, and 18 min—the polyphenol yield reached 213.02 mg GAE/g, demonstrating the green extraction potential of this method (Tebbi et al. 2023).

Similarly, UAE using lactic acid-based solvents for polyphenols extraction from *P. lentiscus* leaves revealed that solvent concentration was a critical factor in yield. A maximum yield of 115.84 mg GAE/g was obtained using 67.5% lactic acid, with lower yields observed at concentrations of 22.5% and 90%. The addition of water enhanced polyphenols recovery, emphasizing the importance of solvent polarity (Zaidi et al. 2024).

Further studies have compared UAE with conventional solvent extraction (CSE) for phenolic extraction from *P. lentiscus* leaves. The optimal UAE conditions were at 13.79 min of extraction time, 33.82% ultrasound amplitude, and 30.99% ethanol, which resulted in a total phenolic content (TPC) of 140.55 mg GAE/g. In contrast, the CSE method required 120 min to achieve comparable results. This indicates that UAE is a more time-efficient extraction method with similar or even superior yields (Dahmoune et al. 2015).

In addition, optimization studies on UAE for polyphenols extraction from *P. lentiscus* fruit cake (defatted residue) and leaves revealed different optimal conditions for each matrix. For fruit cake, the best conditions included: 50% Ethanol at 60 °C for 86 min, yielding an extract with significant antioxidant activity (IC_{50} = 61.79 µg/mL). For leaves, 50% ethanol at 50 °C for 15 min resulted in the highest flavonoid content (10.2 mg/g DW), while 40% ethanol was optimal for maximizing tannin content (40.2 mg/g DW). UAE reduced ethanol consumption by 25% and halved the extraction time compared to traditional methods, underscoring its efficiency in improving yield, minimizing solvent use, and enhancing process sustainability (Detti et al. 2020; Ouatmani et al. 2024).

Microwave-assisted extraction (MAE)

MAE is an efficient method for extracting bioactive compounds from plant material, particularly phenolics and terpenes. This technique is particularly advantageous for heat-sensitive bioactive compounds, such as phenols and α-pinene, which are abundant in *P. lentiscus* and are prone to degradation under conventional extraction conditions (Suktham et al. 2021).

Studies have demonstrated the effectiveness of MAE in optimizing the recovery of these bioactive compounds.

For instance, under specific conditions—46% ethanol level, 500 W microwave power, 60 s of irradiation, and a solvent-to-sample ratio of 28 mL/g—MAE achieved a TPC yield of 185.69 mg GAE/g DW, highlighting the method's efficiency in maximizing phenolics recovery (Dahmoune et al. 2014). Moreover, the phenolic content in both leaves and fruits was found to increase with extraction time, peaking at 12 min before declining due to degradation processes such as oxidation and polymerization. The optimal conditions for leaf extraction were identified as follows: 69 °C, 512 W, and 12 min, while for fruit extraction, the best results were obtained at 75 °C, 602 W, and 15 min (Elez Garofulic et al. 2020).

In addition to phenolics, MAE was compared with other extraction methods, such as hydro-distillation (HD), for essential oil extraction. MAE outperformed HD, particularly in terms of antibacterial activity, as it yielded higher concentrations of terpenes like α-pinene and β-phellandrene (Beraich et al. 2025).

Supercritical fluid extraction (SFE)

SFE using CO_2 as the primary solvent has become an effective and versatile method for extracting active compounds from *P. lentiscus* resin favored as clean solvent free method. Under supercritical conditions, CO_2 combines the liquid-like density (enhancing solubility) and gas-like viscosity (facilitating mass transfer), enabling the efficient extraction of target compounds (Da Silva et al. 2016). This dual characteristic allows for the extraction of both volatile and heat-sensitive bioactive substances, making SFE particularly suitable for preserving delicate aroma compounds and bioactive materials (Sun et al. 2020).

The versatility of SFE lies in its ability to separate various classes of compounds by adjusting operational parameters such as pressure, temperature, and solvent modifiers like ethanol. For example, at 90 bar, a matrix-to-cellulose ratio of 2:1 was found optimal for maximizing batch size without affecting yield (1–1.1%), favoring the extraction of monoterpenes (e.g., α-pinene and β-pinene) and oxygenated monoterpenes (e.g., verbenone and pinocarvone). Triterpene acids were efficiently extracted in the presence of 3% ethanol and by increasing pressure to 200 bar, yielding 26.6% with an acid value of 15.6. Higher pressures (e.g., 120 bar) favored the recovery of sesquiterpenes, such as caryophyllene oxide, demonstrating the selective extraction capabilities of SFE for different compound classes (Xynos et al. 2018).

Further studies have explored the influence of CO_2 pressure, flow rate, density, and particle size on extraction efficiency from *P. lentiscus* leaves (Aydi et al. 2020). At a pressure of 220 bar, a CO_2 flow rate of 0.602 kg/h, and a particle size of 220 µm, extraction efficiency reached a maximum of 0.285%. Major compounds identified included α-pinene (32%) and terpinene-4-ol (13%), showcasing the optimized SFE conditions' effectiveness for preparing terpene-rich extracts.

Comparative studies highlighted the advantages of SFE over other extraction methods. For instance, SFE at 50 °C and 300 bar demonstrated superior preservation of bioactivity compared with high-pressure extraction at 90 °C for 8 h (Choi et al. 2022). The supercritical extract exhibited significant antiproliferative activity against oral cancer cells (MC3 and HN22), reducing survival rates to 49% and 45%, respectively, at a concentration of 40 µg/mL. In contrast, high-pressure extraction showed weaker inhibition, with survival rates of 80%, 75%, and 67% at similar concentrations.

Additionally, SFE was found effective for preserving heat-sensitive compounds such as D-limonene and α-bisabolol. At 90 bar and 45 °C, GC–MS analysis identified 40 compounds predominated by *tau*-cadinol, palmitic acid, and germacrene D. These extracts demonstrated exceptional antioxidant activity (DPPH IC_{50} = 13.28 ± 0.2 mg/mL), outperforming MAE (IC_{50} = 17.24 ± 0.1 mg/mL) and hydro-distillation (IC_{50} = 23.71 ± 0.3 mg/mL), as well as potent antibacterial activity (minimum inhibitory concentration = 60.21 µg/mL) (Beraich et al. 2025).

Comparative assessment and preferred extraction methods

While each method offers distinct advantages, a comparative analysis reveals that the "preferred route" for *P. lentiscus* is highly dependent on the target metabolites and required efficiency. Based on the integrated data, UAE is currently the most recommended technique for general polyphenol

recovery due to its superior balance of high TPC yield (e.g., ~ 140.55 mg GAE/g) and time efficiency, reducing processing time by over 85% compared to conventional solvent extraction. For high-value, heat-sensitive compounds such as terpenes of essential oils (e.g. D-limonene), SFE is the preferred route as it ensures maximum bioactivity preservation and a solvent-free final product, outperforming MAE and hydro-distillation in antioxidant activity (IC_{50} = 13.28 mg/mL). Lastly, for large-scale screenings where equipment cost is a primary factor, SE using water as a solvent on fresh leaves remains the most effective traditional route.

Authentication and quality control aspects of *P. lentiscus* products

Detection of adulteration in CMG and its authentication has been challenging due to the difficulty of sample handling (because of poly-β-myrcene polymer) and the lack of commercial standards of its unique metabolites (especially MNA and IMNA) (Pachi et al. 2020). Adulterated products are characterized by packing falsification and/or added resins with inferior economic value, such as Iranian mastic (*Pistacia atlantica*), *Pinus,* and *Boswellia* (frankincense) (Pachi et al. 2021). The European pharmacopeia authenticate CMG deepening on its essential oil content *via* qualitative thin layer chromatography (TLC) and distillation yield of minimum 10 mL essential oil/kg dry resin, without quantification of any markers or consideration of its triterpenes in this official method (Pachi et al. 2020).

The high performance thin layer chromatography (HPTLC) is a more advanced version from TLC that is characterized by process automation as well as better resolution and reproducibility (Do et al. 2015). Accordingly, Pachi et al. employed HPTLC to profile CMG samples and their respective oils following the pharmacopeia procedures. They observed dark brown spots concentrated on the baseline in official method. Hence, they suggested the following modifications in their in-house method: (1) dichloromethane and methanol (98:2 v/v) instead of light petroleum and toluene (5:95 v/v) as a mobile phase. (2) reducing the initial concentration from 100 mg/mL to 10 mg/mL for crude mastic powder (Pachi et al. 2021).

Chiral GC analyses is a technique that can identify enantiomer types which are specific for each natural source and any alteration in their values may refer to an adulteration process (Do et al. 2015). In this context, a study proposed the ratios of (−)/(+)-α-pinene ($\leq$ 1:100) and (−)-α-pinene/myrcene (1.9:100–11:100) as markers for authenticity of CMG oils (Paraschos et al. 2016). Another study explored the combination of olfactory detection and enantiomeric ratios of key odorant components in CMG. The chief volatile component (+)-α-pinene (*R*/*S* % = 99.6/0.4) and minor components β-myrcene, limonene (37.8/62.2), β-linalool (4.3/95.7), and perillene were the most contributors to mastic aroma (Rigling et al. 2019).

Targeting triterpenes, Jin et al. suggested a quantitative method for oleanonic acid as a marker in CMG samples using HPLC–UV (Jin et al. 2017). Another study applied high-performance liquid chromatography-evaporative light scattering detector (HPLC-ELSD) to determine MNA and IMNA in CMG samples as specific markers in addition to other triterpenoids (Svingou et al. 2023). The study used ELSD over UV or photo diode array (PDA) detectors as it is an universal tool can be used for analysis of the triterpenes class that lacks chromophores and hence has very low UV absorption (Lesellier et al. 2012; Vilkickyte and Raudone 2021). The study confirmed ELSD superiority over PDA revealing 9.4–18.8% MNA (13.4% on average), 5.5–14.2% IMNA (9.7%), and 10.8–15.7% oleanonic acid/moronic acid (13.5%) in CMG samples (Svingou et al. 2023).

In conclusion, advanced techniques such as HPTLC and HPLC-ELSD offer robust potential for developing validated methods to authenticate CMG.

Delivery systems and applications of *P. lentiscus* extracts

Pistacia lentiscus and its derivatives, such as essential oils and resin, demonstrate extensive therapeutic potential as antimicrobial, anti-inflammatory, antioxidant, and anticancer agents (Rauf et al. 2017). However, their practical use is limited by poor solubility, low bioavailability, and inadequate stability. To address these issues, various delivery systems have been developed to enhance stability, solubility, release characteristics, and targeting capabilities of *P.*

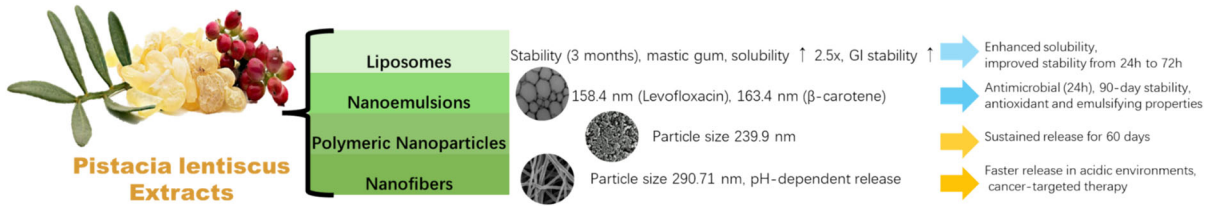


Fig. 4 *P. lentiscus* novel delivery systems with their characteristics and applications

lentiscus extracts (Alabrahim and Azzazy 2025), as summarized in Fig. 4. Liposomes have proven effective as drug delivery systems for *P. lentiscus* extracts. A study utilizing soy lecithin and ecofriendly solvents successfully prepared stable, uniformly dispersed liposomes containing lentisk oil. These liposomes not only mitigated oxidative damage to keratinocytes and fibroblasts caused by hydrogen peroxide but also promoted wound healing. At a concentration of 30 mg/mL, the liposomes remained stable for three months under storage conditions, demonstrating their robustness and potential for long-term use (Allaw et al. 2021).

Advances in plant extract encapsulation technologies have focused on liposomal formulations to enhance the solubility, bioavailability, and stability of bioactive compounds. Recent studies highlight the encapsulation of acidic and neutral mastic gum extracts into liposomes, demonstrating significant potential to improve their functional properties. These formulations improved solubility and bioavailability by 2.5-fold and twofold, respectively. The acidic mastic gum extract (AMGE) liposomes-maintained stability for over 72 h under simulated gastrointestinal conditions, compared with less than 24 h for the unencapsulated extract. Moreover, AMGE liposomes demonstrated significant antibacterial effects against *Staphylococcus aureus* (inhibition zone: 20 mm) and *Pseudomonas aeruginosa* (18 mm), reducing their viability to 28% at 50 µg/mL, compared with 65% for the unencapsulated extract (Gortzi et al. 2022).

Microencapsulation has also been employed, with shikonin encapsulated into mastic resin-derived microcapsules showing enhanced stability and controlled release properties. Particle size and encapsulation efficiency were optimized, establishing this method as a viable potential option for the improved delivery of bioactive compounds (Kravva et al. 2008). Similarly, nanoemulsions combining lentisk oil with antibiotics such as levofloxacin achieved particle sizes around 158.4 nm, with sustained antibacterial activity against *Staphylococcus aureus* for over 24 h (Maurizi et al. 2024). Another study prepared β-carotene-rich nanoemulsions using 75% ethanol-extracted lentisk components, with average particle sizes of 163.4 nm. These nanoemulsions exhibited excellent stability over 90 d and demonstrated dual antioxidant and emulsifying functionalities (Feki et al. 2023).

Polymeric nanoparticles have also been developed, utilizing polylactic acid as a shell material for encapsulating lentisk oil. The resultant nanoparticles had a particle size of 239.9 nm, polydispersity index of 0.081, and encapsulation efficiency of 37.45%, with sustained release observed over 60 d (Vrouvaki et al. 2020). Niosomes, another delivery platform, showed enhanced cytotoxic effects of lentisk oil against breast cancer cells by *ca.* tenfold, demonstrating the potential for targeted cancer therapies (Fahmy et al. 2023). Nanofiber technology has further expanded the scope of lentisk oil applications. Poly-ε-caprolactone nanofibers loaded with lentisk oil and 5-fluorouracil exhibited diameters ranging from 290.71 nm to 680.95 nm. These nanofibers remained stable over 42 d and showed pH-dependent release, with higher release rates in acidic environments (pH 5.4), highlighting their suitability for cancer-targeted drug delivery (Alabrahim and Azzazy 2024).

Natural biopolymer matrices like mastic gum have recently garnered attention in pharmaceutical applications. For instance, mastic gum has been used in mucoadhesive microspheres for gastric drug delivery. When combined with amoxicillin trihydrate, mastic gum modulated particle sizes (35.2–48.1 µm) and swelling indices (58.6–74.3), providing sustained release and high mucoadhesive efficiency, enabling effective treatment against *H. pylori* infections (Mundarinti and Ahad 2023).

In summary, *P. lentiscus* extracts have been effectively incorporated into diverse delivery systems,

significantly enhancing their stability, bioavailability, and therapeutic potential for various applications.

Conclusion and future directions

In conclusion, *P. lentiscus* and its byproducts, particularly CMG, exhibit potential for applications in medicine, industry, and food technology due to their diverse phytochemical composition. The variability in secondary metabolites is influenced by several factors, such as environmental conditions, seasonal changes, plant organs, gender, and cultivation methods, highlighting the importance of understanding these variables to optimize bioactive compounds' production. Advanced extraction techniques such as UAE, MAE, and SFE improved efficiency, sustainability, and quality compared with traditional methods. Authentication of *P. lentiscus* products remains a critical challenge, with modern analytical techniques such as HPTLC and HPLC-ELSD enhancing the capability to differentiate authentic CMG products from adulterated ones. Furthermore, innovative delivery systems, including liposomes, nanoemulsions, polymeric nanoparticles, and nanofibers, significantly improve stability, bioavailability, and targeted delivery of *P. lentiscus* extracts, expanding their therapeutic applications. Future research should focus on the untapped bioactivities of metabolites, optimizing extraction sustainability, standardizing authentication protocols, and scaling up production to meet industrial demands, ensuring the full utilization of *P. lentiscus* as a valuable resource in healthcare and food industry fields.

Author contribution Mohamed A. Anwar: Writing—original draft, Visualization, Investigation, Data curation. Yuting Fu: Writing—original draft, Visualization, Investigation, Data curation. Haroun Khan: Writing—review & editing, Validation, Supervision. Mohamed A. Farag: Writing—review & editing, Visualization, Validation, Supervision, Resources, Conceptualization.

Data availability Not applicable.

Declarations

Competing interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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