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Ethnobotany, phytochemistry, and biological properties of three naturally associated Mediterranean species

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ABSTRACT

Chamaerops humilis (*C. humilis*), *Olea europea var Sylvestris* (*O. oleaster*), and *Asparagus albus* (*A. albus*) are three plant species native to the Mediterranean basin. They are often associated in nature. In different countries of the Mediterranean area, they are used in folk medicine in order to treat several ailments, such as urinary, digestive, respiratory, neurologic, and metabolic diseases. The numerous traditional therapeutical uses of these three plant species have led to the completion of several studies demonstrating scientifically their biological activities. However, as regards *A. albus*, only a few studies were carried out in this context. This review has the objective of documenting and analyzing different works concerning the ethnomedicinal uses, chemical composition, and bioactive potential of these three medicinal plants, in order to provide researchers with a global database of biological properties that have been demonstrated and to identify gaps for further studies. The electronic databases used for data collection are Google Scholar, Pub Med, Pub Chem, Science Direct, and Scopus. The results of this study show that thanks to their richness in bioactive compounds, *C. humilis*, *O. oleaster,* and *A. albus* exhibit several biological activities that can be exploited in the medical and agro-food fields.

INTRODUCTION

The use of medicinal and aromatic plants in the agri-food and medical fields has emerged as a sustainable solution permitting to overcoming of adverse effects related to synthetic food additives and chemical medicines [1,2]. Ethnobotanical studies play an important role in the discovery of medicinal and aromatic plants used by different populations for their healing potential [3]. Indeed, these studies open the way for researchers to utilize the documented ethnobotanical data for the study of the biological activities of the mentioned medicinal and aromatic plants [4–7], in order to exploit their activities for sustainable practical applications, including the use of plants extracts, essential oils or isolated molecules, as green compounds in different fields such as the food industry, medical, and agricultural sectors.

Chamaerops humilis, *Olea oleaster,* and *Asparagus albus,* are three plant species belonging to *Arecaceae*, *Oleaceae*, and *Liliaceae* families, respectively [8,9]. They are naturally distributed in the Mediterranean basin [10–12], in which they are often occurring associated with different areas [13–15]. According to the International Union for Conservation of Nature, they are classified as least concern species [16].

Chamaerops humilis has been traditionally used to treat various ailments such as diabetes, hepatitis, dyspepsia [17] warts [18], bile stones, liver diseases, and diabetes [19]. Different studies have proved the important bioactive potential of *C. humilis.* Thus, this plant was found to exert antioxidant [20–23], antimicrobial [24–27], anticholinesterase [22,28], antidiabetic [29,30], and antiviral properties [31]. The phytochemical screening of this plant has been the subject of several works which revealed the richness of *C. humilis* in bioactive compounds including flavonoids, saponins, esters,

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terpenoids, quinones, phenolic acids, tannins, alcohols, steroids, and alkaloids [21,32–34].

Similarly, the traditional use of *O. oleaster* in the treatment of several diseases [35–38] has led to the performance of many scientific works demonstrating its biological properties including antioxidant [39,40], antimicrobial [41,42], antiviral [41], and hepatoprotective activities [43]. These activities are related to the multiple active compounds that have been revealed through different phytochemical screening tests and methods [39,44,45].

As for *A. albus*, it was also used traditionally in folk medicine against a wide variety of diseases: jaundice, dental ailments, respiratory and rheumatic problems [46], stomach disorders [47], and urinary diseases [48,49]. However, to the best of our knowledge, up to date, only four published works exist regarding its phytochemistry and biological properties [10,50–52].

Thus, the aim of this review is to document and summarize data up-to-date related to *C. humilis, O. oleaster,* and *A. albus* ethnomedicinal uses and phytochemical compounds and to highlight their biological activities, in order to encourage their use in different sectors as green products and to determine gaps for further studies. To the best of our knowledge, no review is available in this context.

MATERIALS AND METHODS

In order to gather data concerning the ethnomedicinal uses of *C. humilis*, *A. albus*, and *O. oleaster*, their phytochemistry and biological properties, a comprehensive search was carried out in different electronic databases including Google Scholar, Pub Med, Pub Chem, Science Direct, and Scopus. All published papers until December 2023 that represent the aim of our review were included. In addition to these three plant species names, the keywords used for this research were: pharmacological properties, antioxidant, antimicrobial, ethnomedicinal, ethnobotanical, phytochemistry, bioactive compounds, dwarf palm, and wild olive. For the Google Scholar engine, we have applied exclusion criteria taking in to account the existence of these keywords only in the title so as to limit the number of obtained results.

In order to visualize the dominant words in the reviewed studies, their titles and abstracts were analyzed by Vosviewer software.

RESULTS AND DISCUSSION

Dominance of studies related to the traditional use, phytochemistry, and bioactivity of the studied plants

According to Figure 1 obtained using Vosviewer software, two important points can be drawn. On the one hand, we note the prevalence of studies concerning the traditional use of these plants in Morocco and Algeria (green circles). On the other hand, studies regarding the bioactivity and phytochemistry of the plants studied are dominant for the two species: *C. humilis* and *O. oleaster* (red circles). Moreover, these studies concern different parts of these plant species (leaf, fruit, and olive pits), and reveal the presence of certain predominant bioactive compounds such as rutin and oleuropein (red circles).

Botanical description and geographical distribution

Chamaerops humilis

Chamaerops humilis is naturally distributed in Africa and Europe and constitutes an important floristic element of the western Mediterranean region [53].

This plant is in general in the form of compact and low clumps. It is characterized by:

- Stipe covered with reticulated fibers, which can reach 6–8 m high in protected places.
- Leaves with fan-shaped blades, reaching 70 × 80 cm split up to 2/3 and more.
- Long petiole 20–40 cm, with generally spiny margins (Fig. 2).

Moreover, male flowers are yellow, females are green, and hermaphrodites are greenish yellow. Etamines have fused nets at the base, free carpels, sessile stigma, ovules erect with basal placentation, and monosperm bay [9].

Olea oleaster

Geographically, *O. oleaster* is distributed in the whole Mediterranean Basin [54].

This plant represents the wild olive tree or shrub, having young, subquadrangular shoots. The leaves are briefly petiolate, simple, opposite, lanceolate, entire, leathery with discolored faces, silvery below and green above. Flowers are hermaphroditic or unisexual, and drupes have thick and bony cores [8] (Fig. 2).

Asparagus albus

Asparagus albus thrives in the Mediterranean region on rocky soils. Precisely, it's distributed naturally in

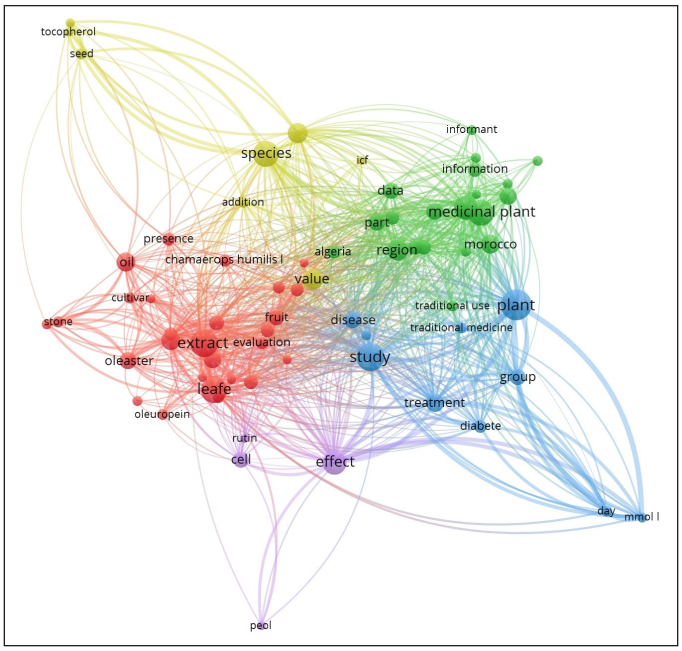

Figure 1. Visualization of dominant studies regarding traditional use, phytochemistry and bioactivity of the studied plants retrieved from different databases (Google Scholar, Pub Med, Pub Chem, Science Direct and Scopus) using Vosviewer software.

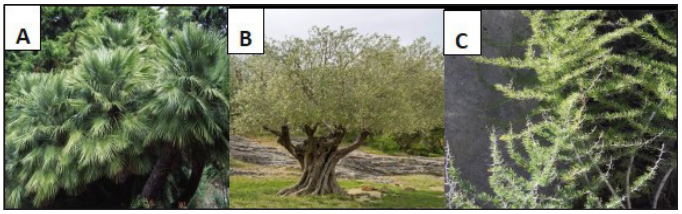

Figure 2. (A) *Chamaerops humilis* ; (B) *Olea oleaster*; (C) *Asparagus albus*.

Northwestern Africa and Southwestern Europe [55]. This plant is characterized by white, fragrant stems and branches, straight or evenly inclined, broad cladodes, usually arched-decurved, slightly thickened claviform, obtusiuscule apex, slightly mucronate. In addition to a curved leaf spur, covered when young with short, dense papillae [9] (Fig. 2).

Ethnomedicinal uses

Chamaerops humilis

Despite the occurrence of *C. humilis* in the Mediterranean region, ethnobotanical documentation of its uses exists only for the two following countries: Algeria and Morocco. Thus, in Algeria, leaf decoction and macerated extract are used against diabetes, hepatitis, and dyspepsia [17,56,57]. Fruits (Powder, decoction, macerated extract, and salad) are taken to fight gingiva, influenza, coughing, asthma, infection of the digestive tract, dyspepsia, breast, brain, and blood cancer [17]. Roots (decoction, powder, and macerated extract) are exploited to treat hepatitis, anemia, intestinal worms, rheumatism, and diabetes, and also for cleaning the uterus after childbirth [17,58]. The palm heart (salad) is eaten against dyspepsia, hypertension, cardiovascular diseases, diabetes [17], bloating, gastric pain, and constipation [56]. The spadicea (salad) is consumed against gastric pain and toning [56]. While the decoction and macerated extract of the heart of palm and spadicea are taken as carminative, and stimulant, against gastritis, gastro-enteritis, gastralgia, diarrhoea, wound of stomach, and constipation [57]. The aerial part infusion is administrated against urinary diseases [59]. In Morocco, leaf decoction is used to heal problems of bile stones, liver diseases, diabetes [19], and respiratory ailments [60]. Fruits (powder, decoction, and raw) are taken against liver diseases, diabetes, bile stones, digestive and urinary disorders, diarrhea, and gingivites [19,60–62]. Roots (decoction, cooked, powder, and infusion) are considered efficient against diabetes [62,63] and neurologic diseases [64]. Heart of palm (raw, salad) is administrated to heal gastrointestinal diseases [60], digestive disorders, cardiovascular system disorders, respiratory system disorders, diabetes, hepatitis, hair loss, and weakening of the immune system [26]. In Eastern Mallorca (Balearic Islands, Mediterranean Sea), leaf lotion is used against warts [18], whereas raw fruits are taken directly as antidiarrheal [18].

Olea oleaster

Olea Oleaster is used in folk medicine by several populations of the Mediterranean region. Thus, in Algeria, leaf decoction or infusion is used to adjust blood pressure [37,38]. In Morocco, different leaf preparations (infusion, decoction, and poultice) are used to treat many ailments, namely diabetes, hypertension, and urinary problems [65], in addition to burns [66], mouth diseases [67], nervousness, and parasitic infections [19]. In Libya, this plant species is used to treat gingivitis, Dyspepsia, Eczema, Constipation, and Earache [68]. In the Iberian Peninsula, leaves infusion or decoction are used to treat hypo or hypertension [35,36], whereas their raw form or decoction is considered as hypotensive, hypoglycemic, and anti-acid medicines [69]. In Turkey, leaves or branches decoction is used as a natural remedy against diabetes or hypertension [70,71].

Asparagus albus

Many ethnobotanical studies have highlighted the traditional use of *A. albus* in different countries of the Mediterranean region for medicinal purposes. Thus, in western Algeria, *A. albus* is used as an appetizer and against jaundice, rheumatism, and stomach disorders [72]. In Morocco, young sprouts are used to treat diabetes [36]. Aerial parts and roots are used to get rid of jaundice, dental ailments, respiratory and rheumatic problems [46]. Leaves infusion is consumed against stomach disorders [47], whereas leaves, stems and roots decoction is used for the treatment of several diseases including kidneys, rheumatism, diabetes, anemia, liver, and urinary ailments [73,74]. In Spain, especially in Granada, tender shoots are used as diuretic [35,75]. In Italy, young shoots decoction is also used as a diuretic [48,49].

Phytochemistry

Several studies have been dedicated to the analysis of chemical compounds present in the extracts of these three Mediterranean plant species.

Tables 1–3 show the chemical compounds identified in different plant parts extracts of *C. humilis*, *O. oleaster,* and *A. albus*, respectively. Moreover, they provide also the collection origin of the plant and the method used for their phytochemistry identification.

Chamaerops humilis has been demonstrated to contain a variety of chemical compounds (Table 1). Thus, flavonoids were revealed to be present in the methanolic, ethanolic, and aqueous extracts of its leaves, drupes, and rachis collected from different areas of the Mediterranean basin [21,34,76–79]. Saponins were found to be present in the methanolic extract of its leaves, stems, and underground parts collected from Tokyo [80]. Esters, namely methyl benzoate were identified in the dichloromethane extract of its leaves collected from France [33]. Terpenoids were demonstrated to exist in different extracts of its plant parts [33,57,81,82]. Quinones, phenolic acids, and tannins were exhibited in organic and aqueous extracts of different parts of *C. humilis* collected from Algeria [21,32,76]. Alcohols and alkaloids were found in the aqueous and dichloromethane extracts of its leaves [32,83].

As for *O. oleaster*, it is also rich in several bioactive compounds (Table 2), namely secoiridoid glycosides including oleuropein and oleoside which are characteristics of oleaceae family [40,41,39,44,45,84–86], secoiridiods aglycon such as oleuropein aglycon and ligstroside aglycon [45,85,87], glycosides [39–41,85,86], phenolic acids [40,41,45,87,88],

Table 1. Chemical compounds of *C. humilis* according to the reported studies.

Identified compounds		Plant part	Extract	Collection origin	Identification method	Reference
Flavonoids						
	Procyanidin, Luteolin 6-C-glucoside 8-Carabinoside, Luteolin-7-O-glucopyranosil-8-C-glucopyrnoside, Orientin, Isoorientin, Apiapigenin-6,8-C glucoside, rutin, luteolin-O Rutinoside, Tricin-7-O-neohesperidoside	Leaves	Methanolic	Algarve	HPLC	[21]
	Catechin, Epicatechin, Proanthocyanidin	Drupes	Methanolic	-	Thin layer chromatography (TLC)	[77]
	Flavone C-glycoside, Tricin 5-glucoside	Leaves	Ethanolic	Lyon, California		[79]
	Tricin, glycosylflavone and leucocyanidin	Leaves	-	Royal Botanic Gardens (U.K)	Ultraviolet Spectroscopy and TLC	[78]
	Luteolin, rutin, kaempferol, hesperidin	Leaves	Aqueous,	Algeria	Liquid Chromatograpy / Electros-pray Ionization / Mass Spectroscopy (LC/ESI-MS/MS)	[76]
	Rutin, kaempferol, hesperidin + other flavonoids in low quantities	Rachis, fruits	Methanolic			
	Quercetin	Leaves	Aqueous	Algeria	TLC	[34]
Saponins						
	Methyl proto-dioscin, Methyl proto-Pb	Stems	Methanolic	Tokyo	Sephadex column chromatography	[80]
	Methyl proto-dioscin, Methyl proto-Pb, Methyl proto-rhapissaponin	Underground parts	Metanolic	Tokyo	Sephadex column chromatography (SCC)	[80]
	Methyl proto-Pb, Tricin7-O-rutinoside	Leaves	Metanolic	Tokyo	SCC	[80]
Esters						
	Methyl benzoate	Leaves	Dichloromethane	France	Gas chromatography -mass spectroscopy (GC/MS)	[33]
Terpenoids						
	Beta-Ocimene, linalool, sesquiterpene, farnescene	Leaves	Dichloromethane	France	GC/MS	[33, 81]
	Tocotrienol	Seeds	Methanolic	-	HPLC	[82]
	Unsaturated terpenoid sterols	Palm heart, spadices, leaves	-	Algeria	Terpenoids screening test	[57]
Quinones						
	Anthraquinones	Fruits	Aqueous	Algeria	Anthraquinones screening test	[32]
	Anthracenosides	Leaves	Methanolic	Algeria	Anthracenosides screening test	[32]
Phenolic acids						
	Quinic, malic, chlorogenic & protocatechuic acids + other phenolic acids in low quantities	Leaves, Rachis, fruits	Aqueous, Methanolic	Algeria	LC/ESI-MS/MS	[76]
	Caffeoylquinic acid (Phenolic acid)	Leaves	Methanolic	Algarve	HPLC	[21]
Tannins						
	Gallic tannins	Leaves, fruits	Methanolic, aqueous, diethyl ether	Algeria	Tannins screening test	[32]

Continued

Identified compounds		Plant part	Extract	Collection origin	Identification method	Reference
Alcohols						
	Quercitol	Leaves	Aqueous	Royal Botanic Gardens, Kew	Crystallographical measurement, melting point, combustion and chemical character	[83]
	Benzyl alcohol	Leaves	Dichloromethane	France	GC/MS	[33]
Alkaloids						
Indole		Leaves	Dichloromethane	France	GC/MS	[32]

HPLC: High performance liquid chromatography; TLC: Thin layer chromatography; LC: Liquid Chromatograpy; ESI: Electrospray Ionization; GC/MS: Gas chromatography - Mass Spectroscopy.

Table 2. Chemical compounds of *O. oleaster* according to the reported studies.

Identified compounds	Plant part	Extract	Collection origin	Identification method	Reference
Secoiridoid glycosides					
Oleosidate-11-methyl ester, iso-leosidate-11-methyl ester, oleuropein glucoside, nuzhenide, oleuropein, nuzhenide 11-methyl oleoside, ligstroside.	Fruits	Methanolic	Taza (Morocco)	HPLC-Diode array detection (DAD)/ ESI/ MS	[39]
Oleuropein	Leaves & branches	Methanolic	Turkey	HPLC	[84]
	Fruits	Hydromethanolic	Portugal	HPLC/DAD	[45]
	Leaves	Aqueous	Greece, spain	HPLC/DAD	[86]
	Leaves	Hydromethanolic extract	Taounate (Morocco)	LC/MS-MS	[44]
	Leaves	Methanolic	Portugual	HPLC	[40]
Oleoside	Fruits	Methanolic	Taza (Morocco)	HPLC-DAD/ESI/MS	[39]
	Fruits	Ethyl acetate	Tunisia	Ultra Performance Liquid Chromatography (UPLC)-ESI-High resolution mass spectrometry (HRMS).	[85]
Hydroxyoleuropein isomers, Oleuropein hexoside, Lucidumoside C	Leaves	Hydroethanolic	Tunisia	LC-DAD-ESI-MS	[41]
Lucidumoside derivative	Fruits	Ethyl acetate	Tunisia	UPLC-ESI-HRMS	[85]
Secoiridoids					
Ligstroside aglycone, 10-Hydroxy oleuropein aglycone, Methy-oleuropein aglycone, Oleuropein aglycone	Fruits	Hydromethanolic	Algeria	HPLC-DAD-MS	[87]
Oleuropein aglycon (and derivatives), Ligstroside Aglycon and derivatives	Fruits	Hydromethanolic	Portugal	HPLC/DAD	[45]
Hydroxy-oleuropein aglycon, Dehydrogenated Ligstroside aglycon, Hydrogenated oleocanthalic acid, Oleuropein aglycon, Ligstroside aglycon, Hydroxy-O-decarboxymethyl oleuropein aglycon	Fruits	Ethyl acetate	Tunisia	UPLC-ESI-HRMS	[85]
Glycosides					
Hydroxytyrosol-O-glucoside, verbascoside	Fruits	Methanolic	Taza (Morocco)	HPLC-DAD-ESI/MS	[39]
Verbascoside	Leaves	Methanolic	Portugual	HPLC	[40]
	Leaves	Aqueous	Greece, spain	HPLC/DAD	[86]
Decaffeoylverbascoside	Leaves	Hydroethanolic	Tunisia	LC-DAD-ESI-MS	[41]

Continued

Identified compounds	Plant part	Extract	Collection origin	Identification method	Reference
Loganicacid glucoside	Fruits	Ethyl acetate	Tunisia	UPLC-ESI-HRMS	[85]
Phenolic acids					
Coumaric acid	Fruits	Hydromethanolic	Algeria	HPLC-DAD-MS	[87]
Gallic acid, Hydroxybenzoic acid, Protocatechuic acid, Vannilic acid	Leaves	Methanolic	Portugual	HPLC	[40]
Coumaric acid, Cinamic acid, Ferulic acid	Fruits	Hydromethanolic	Portugal	HPLC/DAD	[45]
Dicaffeoylquinic acid, Gallagic acid	Leaves	Hydroethanolic	Tunisia	LC-DAD-ESI-MS	[41]
Chlorogenic acid, Caffeic acid	Leaves	Methanolic	Algeria	HPLC	[88]
Flavonoids					
Rutin, luteolin-7-glucoside, luteolin-4-glucoside,	Fruits	Methanolic	Taza (Morocco)	HPLC-DAD-ESI/MS	[39]
Eriodictyol, Luteolin, Naringenin, Apigenin, Methoxy-luteolin	Fruits	Hydromethanolic	Algeria	HPLC-DAD-MS	[87]
Apigenin-7-O-glucoside, Epigallocatechin, Luteolin-7-O-glucoside, Rutin	Leaves	Methanolic	Portugual	HPLC	[40]
Luteolin, Apigenin, Methyl-Luteolin	Fruits	Hydromethanolic	Portugal	HPLC/DAD	[45]
Epicatechin, Luteolin-7-O-rutinoside, Luteolin-7-O-glucoside, Rutin, Apigenin-7-O-rutinoside,	Leaves	Hydroethanolic	Tunisia	LC-DAD-ESI-MS	[41]
Rutin, Quercetin, 5,3′,4′-trihydroxyflavone, Kaempferol.	Leaves	Methanolic	Algeria	HPLC	[88]
Apigenin-7-O-glucoside	Leaves	Aqueous	Greece, spain	HPLC/DAD	[86]
Apigenin-7-O-rutinoside, Apigenin-7-O-hexosyl3-O-rhamnosides	Fruits	Ethyl acetate	Tunisia	UPLC-ESI-HRMS	[85]
Amentoflavone, Quercetin-3-O-glucoside, Quercetin-3-O-glucoside, Luteolin-7-O-glucoside, Rutin	Leaves	Hydromethanolic extract	Taounate (Morocco)	LC/MS-MS	[44]
Polyphenols					
Hydroxytyrosol	Fruits	Methanolic	Taza (Morocco)	HPLC-DAD-ESI/MS	[39]
	Leaves	Aqueous	Greece, spain	HPLC/DAD	[86]
Hydroxy-tyrosol, Tyrosol	Fruits	Hydromethanolic	Algeria	HPLC-DAD-MS	[87]
	Fruits	Hydromethanolic	Portugal	HPLC/DAD	[45]
	Fruits	Ethyl acetate	Tunisia	UPLC-ESI-HRMS	[85]
Terpenes					
Limonene, Fenchone, (Z)-3-Nonen-1-ol, Copaene, 2-Nonen-1-ol, Caryophyllene, Caryophyllene oxide Ionone, Farnesene	Leaves	volatiles fractions	Portugual	HPLC	[40]
Secologanoside, Oleanolic acid	Leaves	Hydroethanolic	Tunisia	LC-DAD-ESI-MS	[41]
Oleanolic acid, Maslinic acid	Fruits	Ethyl acetate	Tunisia	UPLC-ESI-HRMS	[85]
Alkanes					
2,4,6-Trimethyloctane, Tetradecane, Undecane, Nonadecane, 2,6-Dimethylheptadecane	Leaves	volatiles fractions	Portugual	HPLC	[40]
Ethers					
Methyl chavicol, E-Anethole	Leaves	volatiles fractions	Portugual	HPLC	[40]
Esters					
Methyl salicylate	Leaves	volatiles fractions	Portugual	HPLC	[40]
Hydroxytyrosol acetate	Fruits	Hydromethanolic	Portugal	HPLC/DAD	[45]
	Fruits	Ethyl acetate	Tunisia	UPLC-ESI-HRMS	[85]
Sitosteryl ferulate	Leaves	Hydroethanolic	Tunisia	LC-DAD-ESI-MS	[41]
Aldehydes					
Tolualdehyde, Decanal, (E)-2-Decenal, (E, E)-2,4-Decadienal	Leaves	volatiles fractions	Portugual	HPLC	[40]

Continued

Identified compounds	Plant part	Extract	Collection origin	Identification method	Reference
Vanillin	Fruits	Hydromethanolic	Portugal	HPLC/DAD	[45]
Tannins					
Valoneic acid dilactone, Diellagilactone	Leaves	Hydroethanolic	Tunisia	LC-DAD-ESI-MS	[41]
Ketones					
Acetophenone, Isophorone, Damascenone	Leaves	volatiles fractions	Portugal	HPLC	[40]

HPLC: High performance liquid chromatography; DAD: Diode array detection; ESI: Electrospray Ionization; MS: Mass Spectroscopy; LC: Liquid Chromatograpy; UPLC: Ultra Performance Liquid Chromatography; HRMS: High resolution mass spectrometry.

Table 3. Chemical compounds of *A. albus*.

Identified compounds	Plant part	Extract	Collection origin	Identification method	Reference
Flavonoids					
Catechin, rutin, quercetin	Leaves	Aqueous	Tunisia	HPLC	[52]
Asterin, rutin, nicotiflorin, narcissin, epicatechin gallate, Quercetin.	Shoots	Ethanolic	Spain	HPLC/DAD; LC/MS	[50]
Phenolic acids					
Gallic acid, 3,4-dimethoxybenzoic acid, vanillic acid	Leaves	Aqueous	Tunisia	HPLC	[52]
Coumaric acid, Syringic acid, 5-O-p-coumaroyl quinic acid	Shoots	Ethanolic	Spain	HPLC/DAD; LC/MS	[50]

HPLC: High performance liquid chromatography; DAD: Diode array detection; LC: Liquid Chromatograpy; MS: Mass Spectroscopy.

flavonoids [39–41,44,45,85–87], and polyphenols [39,45,85,86]. In addition to these compounds which were found in different extracts of *O. oleaster* collected from several countries of the Mediterranean basin, terpenes and esters were revealed in extracts of this plant collected from Portugal and Tunisia [40,41,85] whereas aldehydes and ketones were revealed in the extracts of *O. oleaster* leaves and fruits collected from Portugal [40,45].

Regarding *A. albus*, only a few works in Tunisia and Spain have been dedicated to the determination of its phytochemistry. Indeed, three flavonoids have been found in its leave's aqueous extracts, namely catechin, rutin, and quercetin [52], whereas for the same plant part, in addition to quercetin and rutin, ethanolic extract was revealed to contain other flavonoids: Asterin, nicotiflorin, narcissin and epicatechin gallate [50]. Moreover, this extract contained also several phenolic acids: Coumaric acid, Syringic acid, and 5-O-p-coumaroyl quinic acid [50]. *A. albus* leaves aqueous extract was found to include other phenolic acids: Gallic acid, 3,4-dimethoxybenzoic acid, and vanillic acid [52].

Overall, these plant species are rich in a wide variety of bioactive compounds, moreover, as it was noted for other plants, their chemical composition varies according to different factors such as the solvent of extraction, the collection origin, and the plant part [5].

Biological activities

Different biological activities were revealed to be exerted by the studied plant species (Fig. 3). Thus, *C. humilis* was found to exhibit antioxidant, antimicrobial, antilithiasic, antidiabetic, neuroprotective, and antiviral activities. *Olea oleaster* was demonstrated to have antioxidant, antimicrobial, antidiabetic, antiviral, hepatoprotective, antihyperlipidemic, and cytotoxic activities. As for *A. albus*, to the best of our knowledge, only three biological activities were proved scientifically, namely, antioxidant, antimicrobial, and hepatoprotective properties.

Antioxidant activity

Concerning the antioxidant activity of extracts of the three medicinal plant species: *C. humilis*, *O. oleaster*, and *A. albus*, several studies have shown the antioxidant activity of extracts obtained from *C. humilis* and *O. oleaster* different parts, whereas only very few studies have been published for *A. albus* (Table 4).

Thus, concerning *C. humilis*, Khoudali *et al.* [89] investigated the antioxidant capacity of *C. humilis* leaves methanolic extract using 2,2-diphenyl-1-picrylhydrazil (DPPH) scavenging test. The obtained results indicated a high ability of the tested extract to scavenge DPPH radicals (median inhibitory concentration IC_{50} = 24.5 µg/ml). Although Benahmed-Bouhafsoun *et al.* [20] tested the antioxidant activity of *C. humilis* using the same extract and method, they obtained an IC_{50} = 180.71 µg/ml. The difference noted in the antioxidant activity between these studies can be attributed to the chemical composition of each studied sample which varies with several factors such as the the geographical origin of the plant, the harvest period, environmental conditions, genotype, and so on.

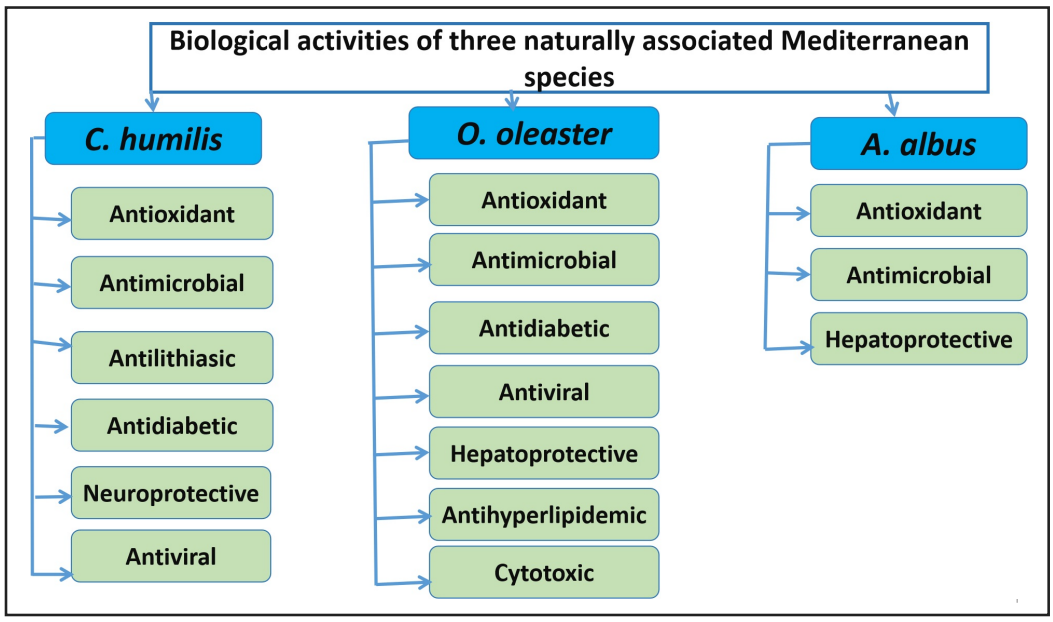

Figure 3. Biological activities of *C. humilis*, *O. oleaster* and *A. albus*.

Coelho *et al.* [21] have also investigated the antioxidant capacity of *C. humilis* leaves methanolic extract using different methods: DPPH (IC_{50} = 0.455 ± 0.087 mg/ml), 2,2-azinobis 3-ethyl-benzothiazoline-6-sulphonate (ABTS): IC_{50} = 0.354 ± 0.082 mg/ml and ferric-reducing antioxidant power (FRAP) assay; and thereby demonstrated a strong reducing power increasing with the extract concentration. The analysis of the chemical composition of this extract using high-performance liquid chromatography (HPLC) has revealed the presence of C- and O- flavones as well as its O-methylated derivatives [21]. These phenolic compounds may be responsible for the antioxidant activity of *C. humilis* leaves methanolic extract.

As regards *C. humilis* leaves aqueous extract, it has been shown [34] to exhibit also an ability of DPPH free radicals scavenging (IC_{50} = 94.55 ± 3.42 µg/ml), probably thanks to its polyphenols (25.20 ± 0.46 mg gallic acid equivalent (GAE)/ g of dried extract (DE)) and flavonoids (17.26 ± 0.61 mg catechin equivalent (CE)/g DE) content. Bouhafsoun *et al.* [28] investigated the antioxidant activity of leaves and fruits methanolic and aqueous extracts using two methods namely ABTS and cupric reducing antioxidant capacity (CUPRAC). The results showed that *C. humilis* leaves methanolic extract exhibited the highest ABTS scavenging (50.11%), whereas fruits induced the strongest antioxidant activity in CUPRAC assay. Thus, it can be concluded that the antioxidant activity of plant extracts depends on many factors involving the solvent used, plant organ, and the test performed. In another study, Miguel *et al.* [90] investigated the antioxidant activity of *C. humilis* aerial parts ethanolic extract and found an IC_{50} = 2.163 ± 0.120 mg/ml, IC_{50} = 0.035 ± 0.079 mg/ml, IC_{50} = 0.035 ± 0.061 mg/ml, IC_{50} = 0.4220 ± 0.004 mg/ml, and an IC_{50} = 0.217 ± 0.013 mg/ml for thiobarbituric acid reactive species (TBARS), ABTS, DPPH, hydroxyl radical scavenging and chelating ferrous ions tests, respectively. The antioxidant capacity of *C. humilis* leaves ethanolic, chloroformic, and aqueous (decocted, infused, and macerated) extracts has been studied by Lachkar *et al.* [26]. The results showed that the ethanolic extract exhibited the highest antioxidant capacity in the different tests performed: DPPH (IC_{50} = 31.18 ± 0.66 µg/ml), ABTS (108.28 ± 1.29 mg equivalent ascorbic acid (EAA)/g extract (E)), FRAP (148.85 ± 0.43 mg, trolox equivalent (TE)/g E), reducing power (10.86 ± 0.01 mg E AA/g E) and hydrogen peroxide (H_2O_2) scavenging (37.34% ± 0.55%) assays. The antioxidant potential of this extract was revealed to be correlated to its high polyphenols (100.27 ± 0.66 µg GAE/mg E) and catechic tannins content (52.11 ± 0.24 µg CE/mg E). More interestingly, Belhaoues *et al.* [24] studied the antioxidant activity of *C. humilis in* different fractions obtained from leaves and fruits: dichloromethane fraction (DCMF), ethyl acetate fraction (EAF), n-butanol fraction (BF), and water fraction (WF). *Chamaerops humilis* leaves EAF exhibited the highest DPPH radical scavenging (IC_{50} = 0.12 mg/ml), ferric reducing activities (0.19 mg/ml), and beta carotene bleaching (66.24%) activities. This important antioxidant ability of *C. humilis* leaves EAF could be related to its richness in phenolic compounds (214.80 ± 3.26 mg GAE/g fraction) in comparison with the other fractions [24]. Moreover, all the obtained fractions from *C. humilis* leaves exhibited a higher antioxidant activity than those obtained from its fruits. These results may be explained by the abundance of phenolic compounds in leaves [24]. This result may be explained by the abundance of phenolic compounds in leaves [24]. The study of the effect of the extraction technique (soxhlet and cold maceration using methanol) was carried out by Eddahhaoui *et al.* [91]. The parts tested were fruits (pulp and seeds). Seed extract obtained by cold maceration exhibited the highest antioxidant activity: IC_{50} = 137.55 ± 0.85 µg ml^{-1}, IC_{50} = 22.14 ± 0.60 µg ml^{-1}, and IC_{50} = 0.99 ± 0.01 µg m^{-1}, for FRAP, ABTS, and DPPH assays, respectively. In fact, it was reported that cold maceration allows a good solubility of active compounds and prevents them from deterioration [91]. Moreover, seed extract obtained by maceration was richer in secondary metabolites [total phenolic compounds (TPC)= 281.64 ± 0.23 mg GAE/gE, total flavonoid content (TFC)= 74.08 ± 0.71 mg quercetin equivalent (EQ)/ gE, total tannic compounds (TTC) (333.83 ± 0.96 mg CE/g E)]

Table 4. Antioxidant activity of *C. humilis, O. oleaster and A. albus* according to reported works. <AQ5>

Plants	Parts used	Extracts/ fractions	Methods used	Findings	References
C. humilis	Leaves	Methanolic extract.	DPPH scavenging	Median inhibitory concentration (IC50)= 24.5 µg/ml; higher that that of tocopherol (IC50 = 26 µg/ml).	[89]
	Leaves	Methanolic extract.	DPPH	IC50 = 180.71 µg/ml	[20]
	Leaves	Methanolic extract.	- DPPH - ABTS- FRAP	- IC50 = 0.455 ± 0.087 mg/ml. - IC50 = 0.354 ± 0.082 mg/ml. - Strong reducing power increasing with the extract concentration.	[21]
	Leaves	Aqueous extract	- DPPH	IC50 = 94.55 ± 3.42 µg/ml	[34]
	Leaves, Fruits	Aqueous and methanolic extracts.	- ABTS - CUPRAC.	- The highest antioxidant value obtained with leaves methanolic extract (50%) inhibition. - The highest antioxidant value obtained with fruits aqueous extract.	[28]
	Leaves	Aqueous (decocted, infused, macerated) and organic extracts (ethanol, chloroform, hexan) extracts.	- DPPH - ABTS - FRAP. - Reducing power (RP) - Hydrogen peroxide (H2O2) scavenging .	Ethanolic extract exhibited the highest antioxidant capacity in the different tests: - DPPH (IC50 = 31.18 ± 0.66 µg/ml). - ABTS (108.28 ± 1.29 mg equvalent ascorbic acid (EAA)/g extract (E)). - FRAP (148.85 ± 0.43 mg TE/g E) - RP (10.86 ± 0.01 mg E AA/g E). - 37.34% ± 0.55% scavenging H2O2.	[26]
	Aerial parts	Ethanolic extract.	- TBARS. - ABTS - DPPH - Hydroxyl radical scavenging - Chelating ferrous ions	- IC50 = 2.163 ± 0.120 mg/ml - IC50 = 0.035 ± 0.079 mg/ml -IC50 =0.035 ± 0.061 mg/ml -IC50 = 0.4220 ± 0.004 mg/ml - IC50 =0.217 ± 0.013 mg/ml	[90]
	Leaves and fruits	DCMF, EAF, BF & WF.	-DPPH -FRAP - Beta carotene bleaching	Leaves EAF exhibited the highest: -DPPH radical scavenging (IC50 = 0,12 mg/ml) -Ferric reducing activities (0.19 mg/ml) and -Beta carotene bleaching (66.24%) activities	[24]
	Fruits (Pulp and seeds)	- Methanolic extract. - Hexane extract.	-FRAP -ABTS -DPPH	- IC50 = 137.55 ± 0.85 µg ml−1, -IC50 = 22.14 ± 0.60 µg ml−1 -IC50 = 0.99 ± 0.01 µg ml−1	[91]
	Leaves, seeds, fruits peel and pulp	- Methanolic extract.	- DPPH - ABTS - FRAP	Seeds extract exhibited the highest antioxidant potential: - IC50 = 81.28 µg ml−1 - 1,440.42 µmol TE/gE - 1,142.46 µmol EAA/gE	[22]
	Seed	Hexane extract.	-DPPH -ABTS	Important antioxidant capacities: - 4.3 mM TE/ g DW- 210 µM TEAC/g (DW)	[23]
oleaster	Fruits	-Oil Methanolic extract.	- DPPH - ABTS - Beta carotene bleaching	Important antioxidant activity in the three tests correlated with the total phenolic and ortho-diphenol content of different populations of O. oleaster	[87]
	Fruits	-Methanolic extract. -Aqueous extract.	- DPPH - ABTS - Metal chelating - FRAP	Methanolic extract exhibited a higher activity in all tests performed.	[39]
	Fruits	-Methanolic extract.	- DPPH	IC50 = 28 ± 0.01 µg/ml	[42]
	Fruits	-Phenolic fractions of ethyl acetate extract.	- DPPH - ABTS	The richer fractions in polyphenols exhibited the best antioxidant activity in DPPH and ABTS assays	[85]

Continued

Plants	Parts used	Extracts/ fractions	Methods used	Findings	References
	Leaves	- Superfluid extract. - Methanolic extract. - Ethanolic extract. -Propanolic extract. - Isopropanolic extract. - Ethyl acetate extract.	-DPPH -Rancimat method -Peroxide value determination	Ethanolic extract exhibited the highest antioxidant activity in the three tests: - DPPH (55.0% ±1.09%). - Racimat method (protection factor of sunflower oil from oxidation = 1.74). -Peroxide determination (a high decrease of peroxide at percentages of 21.5%–49.0% and 17.8%–38.5% in sunflower and olive oils, respectively).	[92]
	Leaves	-Methanolic extract.	-DPPH -FRAP	-IC50 = 62.48 ± 3.71 µg/ml. -FRAP value= 32.66 ± 4.27 (mg TE/g dw)	[40]
	Leaves	-Hydro-methanolic extract. -Hydro-acetonic extract.	-DPPH -FRAP	Hydroacetonic extract exhibited a higher DPPH radical scavenging activity (IC50 = 7.95 ± 0.16 µg/ml).	[93]
	Leaves	-Methanolic extract	-DPPH	IC50 = 106.10 µg/ml.	[88]
	Leaves	-Aqueous extract.	-DPPH. -ABTS.	Variable antioxidant activity between cultivated and wild olive species originating from different geographical areas	[86]
	Stones	- Methanolic extract.	-DPPH -ABTS	Important antioxidant activity of Olea cultivars extracts in comparison with those obtained from Olea wild trees (O. oleaster)	[94]
	-Leaves -Pulps -Stones	-Methanolic extract.	-DPPH -ABTS	Variation in the antioxidant activity of extracts between Olea varieties and between samples of the same variety	[95]
	Leaves Fruits	-Methanolic extract. -Aqueous extract. -Oil.	DPPH	Variation in the antioxidant activity of the different extracts and its correlation with their content in phenols and flavonoids.	[96]
A. albus	Leaves	-Aqueous extract.	- TAC-DPPH -FRAP	-TAC of 34 mg gallic acid equivalent (GAE)/g DW. - IC50 = 47 µg/ ml. -Median effective concentration (EC50)= 97 µg/ ml.	[52]
	Whole plant parts (twigs, bark, roots)	Flavonoids and alkaloids extracts	DPPH	IC50 (1.8 mg/ml) of alkaloids extract lower than IC50 (2.5 mg/ml) of flavonoids extract.	[10]
	Shoots	Ethanolic extract	-DPPH -ABTS	Antioxidant activity of 2.7 ± 1.7 and 2.8 ± 0.7 mmol TE/ 100 g DW in DPPH and ABTS tests, respectively.	[50]
	Leaves, pericarp, rhizome	Ethanolic extract.	-DPPH - FRAP	Pericarp extract has the highest antioxidant activity (26.9 mmol Trolox/kg dw and 66.7 mmol Trolox/kg dw in DPPH and FRAP assays, respectively).	[51]

DPPH: 2,2-diphenyl-1-picrylhydrazil; ABTS: 2,2-azinobis 3-ethyl-benzothiazoline-6-sulphonate; FRAP: Ferric-reducing antioxidant power; CUPRAC: Cupric reducing antioxidant capacity; RP: Reducing power; H_2O_2: Hydrogen peroxide; TBARS: Thiobarbituric acid reactive species; TAC: Total antioxidant capacity; IC_{50}: Median inhibitory concentration; EAA: Equivalent ascorbic acid; E: extract; TE: trolox equivalent; DCMF: Dichloromethane fraction; EAF: ethyl acetate fraction; BF: butanol fraction ; WF: water fraction; DW: dry weight; Gallic acid equivalent: GAE; EC_{50}: Median effective concentration.

than pulp extract obtained by the same method (TPC = 55.81 ± 0.12 GAE/gE, TFC = 15.24 ± 0.53 mg EQ/gE, TTC = 0 mg CE/g E). Gonçalves *et al.* [22] studied the antioxidant activity of *C. humilis* methanolic extract obtained from different parts (Leaves, seeds, fruits peel, and pulp). Seeds extract exhibited the highest antioxidant potential in the different tests used: DPPH (IC_{50} = 81.28 µg ml^{-1}), ABTS (1,440.42 µmol TE/ gE), and FRAP (1,142.46 µmol EAA/gE). This result could be explained by the richness of this extract in condensed tannins and phenolics (170.00 µmol CE/gE and 1,564.88 µmol GAE/gE, respectively) [22]. Furthermore, Mokbli *et al.* [23] investigated the antioxidant ability of *C. humilis* seed oil using the ABTS and DPPH methods. The measured antioxidant capacities were 210 µM TE/g dry weight (DW) for the ABTS test and 4.3 mM TE/g DW for the DPPH assay. These findings revealed the important antioxidant potential of *C. humilis* seed oil wich could be attributed to its high TPC = 91 µg/g oil and TFC = 18 µg/g oil [23].

As for *O. oleaster*, Theodora *et al.* [92] studied the antioxidant potential of different solvents extracts (superfluid, methanolic, ethanolic, propanolic, isopropanolic, and ethyl acetate) of *O. oleaster* leaves using DPPH radical scavenging assay, rancimat method and peroxide value determination. The results revealed that ethanolic extract was the most efficient in

inhibiting DPPH radical. Moreover, this extract exhibited a good capacity in preventing sunflower oil from oxidation in rancimat method and showed a higher ability to protect virgin olive oil and sunflower oil from oxidation in peroxide value determination assay. The high antioxidant power of ethanolic extract could be related to its content in several bioactive compounds including caffeic acid, luteolin, catechin, and oleuropein as it was reported in this study. Moreover, Makowska-Wąs *et al.* [40] and Zighed *et al.* [88] have also demonstrated the antioxidant activity of *O. oleaster* leaves methanolic extract using different assays (DPPH, FRAP) assays, and they have attributed its activity to its content in several phenolic compounds such as rutin, oleuropein, chlorogenic, and caffeic acids. Mezouar *et al.* [93] investigated the antioxidant activity of *O. oleaster* leaves hydromethanolic and hydroacetonic extracts using DPPH and FRAP assays, and found a higher ability of DPPH radicals scavenging for the hydroacetonic extract. Besides they revealed that this extract was richer in polyphenols and flavonoids compared to hydromethanolic extract. In another study, Kabach *et al.* [39] found that methanolic extracts of *O. oleaster* fruits exhibited a higher antioxidant activity than their aqueous extracts in different tests performed (DPPH, ABTS, metal chelating and FRAP assays). This activity probably resulted from the richness of fruits methanolic extract in different phenolic compounds including rutin, verbascoside, oleuropein, and oleoside [39]. Ghazghazi *et al.* [41] also proved the antioxidant capacity of *O. oleaster* fruits methanolic extract which was rich in polyphenols and exerted a DPPH radicals scavenging activity at a low median inhibitory concentration (IC_{50} = 28 ± 0.01 µg/ml). Bouarroudj *et al.* [87] studied the antioxidant ability of methanolic extract obtained from the oil of four populations of *O. oleaster* originating from Algeria. The methods used in their investigation were DPPH, ABTS, and B-carotene bleaching assays. The results obtained showed that methanolic extracts of the four studied populations exhibited an important antioxidant activity in the different used tests. Furthermore, this activity was correlated with total phenolic and ortho-diphenol content of the extracts of the different *O. oleaster* populations. Moreover, a variation in the antioxidant activity of methanolic, aqueous and oil extracts of wild and cultivated Olea trees was oserved by Al-Owamri *et al.* [96], with a correlation between the antioxidant activity of these extracts revealed by DPPH assay and their content in phenols and flavonoids. Besides, Hannachi *et al.* [94] investigated the antioxidant activity of different *O. oleaster* and Olea cultivars stones methanolic extracts using DPPH and ABTS assays. In their study, all extracts exerted an important antioxidant effect, with mean values of 6.88 ± 0.88 and 0.48 ± 0.15 mM TEAC; 12.14 ± 1.72 and 0.61 ± 0.001 mM TEAC for *O. oleaster* and olea cultivars extracts, respectively. These results demonstrate that extracts obtained from Olea cultivars have a higher antioxidant activity in comparison to those obtained from wild Olive trees. This activity could be related to the richness of Olea cultivars extracts in polyphenols and flavonoids [94, 96]. Similarly, Hannachi *et al.* [95] showed the antioxidant activity of leaf, pulp, and stone of two Olea cultivars and two *O. oleaster* trees methanolic extracts using DPPH and ABTS tests. In this study, significant differences in the antioxidant activity and in total polyphenols and flavonoids contents were observed, not only between Olea wild and cultivars trees extracts, but also between extracts of the same variety. These differences could be attributed to the intra-varietal variations. Recently, Martínez-Navarro *et al.* [86] revealed that leaves aqueous extracts of cultivars and Olea wild trees originating from Spain and Greece, exhibited a different antioxidant capacity in DPPH and ABTS tests. These findings allow to suggest that in addition to the intra-varietal variations, the geographical distribution of species also has an influence on their antioxidant activity [5]. More interestingly, Ghorbel *et al.* [85] assessed the antioxidant activity of two phenolic fractions of *O. oleaster* fruits ethyl acetate extract. They found that the richer fraction in polyphenols gived the best antioxidant activity in DPPH and ABTS assays. Moreover, they have attributed the antioxidant activity of this fraction to the presence of the phenolic compound ‘’oleuropein aglycon ‘’ which was absent in the other fraction.

As regards *A. albus,* Hamdi *et al.* [51] assessed the antioxidant activity of *A. albus* leaves, pericarp, and rhizome ethanolic extracts using DPPH and FRAP assays. The results revealed that pericarp extract has a stronger antioxidant activity than the other extracts (26.9 mmol Trolox/kg dw and 66.7 mmol Trolox/kg dw in DPPH and FRAP assays, respectively). Moreover, Serairi-Beji *et al.* [52] assessed the antioxidant activity of *A. albus* leaves aqueous extract using three assays : total antioxidant capacity (TAC), DPPH, and FRAP tests. The results showed that this extract exhibited a good antioxidant effect in all tests performed (TAC = 34 mg GAE/g DW), IC5O of 47 µg/ml and median effective (EC_{50}) of 97 µg/ml in DPPH and FRAP assays, respectively. This activity is probably related to the high content of the tested extract in phenolic compounds including gallic acid, catechin and rutin [52]. In another study, Alami *et al.* [10] investigated the antioxidant activity of alkaloids and flavonoids extracts of *A. albus* using DPPH assay. They found that alkaloids extract exerted a higher antioxidant activity (IC_{50} = 1.8 mg/ml) than flavonoids extract (IC_{50} = 2.5 mg/ml). More recently, Chileh Chelh *et al.* [50] investigated the antioxidant activity of *A. albus* shoots ethanolic extract using DPPH and ABTS assays. Indeed, the tested extract exhibited an important antioxidant activity of 2.7 ± 1.7 and 2.8 ± 0.7 mmol TE/100 g DW in DPPH and ABTS tests, respectively.

Antimicrobial activity

Different studies have demonstrated the antimicrobial potential of these three Mediterranean medicinal plant species.

Concerning *C. humilis,* Lachkar *et al.* [26] investigated the activity of *C. humilis* leaves ethanolic, chloroformic and hexanic extracts obtained by two techniques (maceration and soxhlet extraction) against several bacteria: *Staphylococcus aureus* (*S. aureus*) (CECT976), *Bacillus subtilis* (*B. subtilis*) (DSM6633), *Listeria innocua* (CECT4030), *Escherichia coli* (*E. coli*) K12, *Proteus mirabilis and Pseudomonas aeruginosa (P. aeruginosa*) (CECT118). The results of this study showed that soxhlet extracts induced a better antibacterial activity, with the highest effect obtained against *L. innocua* using chloroformic extract with a minimal inhibitory concentration “MIC” = 1.25 mg/ml. Furthermore, Belhaoues *et al.* [24] demonstrated the susceptibility of various bacteria namely *S. aureus, E. coli, P.*

aeruginosa, Klebsiella pneumoniae, Enterococcus faecalis (*E. faecalis*), and *Salmonella typhimurium* to different solvents fractions obtained from leaves and fruits of *C. humilis*: DCMF, EAF, BF, and WF. The lowest MIC was obtained with leaves EAF against *E. faecalis* (MIC = 0.25 mg/ml).

Hasnaoui *et al.* [25] studied the antibacterial effect of *C. humilis* essential oil against *S. aureus* (SP2VSS2LG), *P. aeruginosa (*7853), *E. coli (*27922), *Listeria monocytogenes (L. monocytogenes*) (15313), and *B. subtilis* (6633). The most sensitive bacteria were *P. aeruginosa, S. aureus,* and *E. coli* (MIC = 250 mg/ml). Besides, *C. humilis* was shown to exhibit also an antifungal activity. Thus, in the study conducted by Okkacha *et al.* [27], *C. humilis* essential oil, and hexanic, chloroformic and aqueous extracts were tested against a panel of mold strains: *Aspergillus flavus* (*A. flavus*), *Aspergillus niger* (*A. niger*), *Aspergillus ochraceus*, *Alternaria. Spp*, *Rhizopus stolonifera,* and *Penicilium viridicatum* and yeasts: *Candida albicans* (*C. albicans*) (ATCC 10231), *C. albicans* (2679), and *C. albicans* (IPP444). A total inhibition of mycelial growth was obtained at the concentration of 2.5 µl for *A. niger*, and at the concentration of 12.5 µl for *A. ochraceus* and *Rhizopus stolonifer.* As for yeasts, the obtained MIC were: MIC = 250 mg/ml for *C. albicans* (ATCC 10231) and *C. albicans* (2679) and MIC = 500 mg/ml for *C. albicans* (IPP444).

As regards *O. oleaster*, Bouchoucha *et al.* [97], tested for the first time the antimicrobial activity of *O. oleaster* aerial parts essential oil. The bacteria tested were *S. aureus ATCC25923 and ATCC 43300, E. coli ATCC 25922, Klebsiella pneumonia ATCC700603, E. faecalis ATCC 51299, P. aeruginosa ATCC27853, B. subtilis ATCC6633.* All these bacteria presented almost the same susceptibility to the essential oil, with an average inhibition zone of 11 mm. The chemical analysis of the essential oil revealed the presence of several compounds including Nonanal, theaspiranea A and 3-hexen-1-ol, benzoate. These compounds could be responsible for the antimicrobial activity. In another study, Ben-Amor *et al.* [41] assessed the antibacterial and antifungal activity of *O. oleaster* leaves hydro-ethanolic extract using micro-dilution method. The results showed that the tested extract exhibited an important antibacterial activity against *S. aureus* strains (ATCC 6538 and ATCC 43300), whereas it did not exert any effect against gram-negative bacteria as well as against the yeast *C. albicans* ATCC 1023. The resistance of Gram-negative bacteria to this extract could be explained by their cell wall structure (rich in Lipopolysaccharides) preventing them from antimicrobial agents.

Djenane *et al.* [98] studied the antibacterial effect of *O. oleaster* leaves hydromethanolic extract on minced beef contaminated by food-borne bacteria: *Salmonella enterica ser. Enteritidis* and Shiga toxin-producing *E. coli* O157:H7. They obtained a significant reduction of pathogenes level after treatment with this extract which was revealed rich in oleuropein. This compound was demonstrated to exert an important antimicrobial activity [99]. Furthermore, Ghazghazi *et al.* [42] studied the antimicrobial activity of fruit pulp methanolic extract of *O. oleaster* against a panel of microorganisms, namely the bacteria: *E. coli* ATCC 8739, *Salmonella typhimurium* NCTC 6017, *S. aureus* ATCC 29213, *P. aeruginosa* ATCC 27853, *Aeromonas hydrophila* EI, *L. monocytogenes* ATCC 7644, and *Bacillus cereus* ATCC 1247, the fungi (*A. niger* and *A. flavus*) and the yeast *C. albicans* ATCC 2091. The results showed that this extract was efficient against all tested microorganisms. Moreover, the minimal MIC value (3.125 mg/ml) was obtained against the two fungi: *A. flavus* and *A. niger*.

Concerning *A. albus,* to the best of our knowledge, up-to date, only two studies have been performed regarding its antimicrobial activity. Thus, Hamdi *et al.* [51] studied the antimicrobial activity of *A. albus* leaves, pericarp, and rhizome antimicrobial activity against several human bacteria, fungi, and resistant bacteria. The results showed that leaves extract was powerful against several bacteria (*L. monocytogenes*, *Enterococcus faecium*, *E. faecalis*, *Streptococcus agalactiae,* and *S. aureus*) and against all fu*ngi: C. albicans, Candida glabrata*, *Candida parapsilosis,* and *Candida tropicalis* (MIC< 1 mg/ml). This antimicrobial activity could be related to the richness of this extract in rutin [51]. More recently, Alami *et al.* [10] tested the antifungal activity of flavonoids and alkaloids of *A. albus* whole plant extracts against *fusarium oxysporum* using poisoned food techniques. The results showed that both flavonoids and alkaloids extracts induced the highest mycellium growth inhibition of 85% which reveals the strong antifungal activity of these extracts.

Antilithiasic activity

Beghalia *et al.* [100] investigated *in vitro* the inhibitory effect of *C. humilis* aqueous extract obtained by infusion against calcium oxalate crystallisation. *Chamaerops humilis* extract used at concentrations of 25% and 50% induced the best inhibition of calcium oxalate crystallization with respective concentrations of 94.86% and 93.07%. The identification of the inhibitory effect was achieved using polarised light photography, in fact, *C. humilis* has affected the aggregation phase and crystals growth. It was suggested that calcium oxalate cristallisation inhibition by plants extracts may be due to their active compounds [101] that affect the potential energy of atoms and prevent them from bonding to each other, inhibiting, therefore, crystals formation [100]. Similarly, Beghalia *et al.* [102] found that *C. humilis* aqueous extract obtained by decoction, exhibited *in vitro* the same inhibition effects of calcium oxalate crystallization: 94.86% and 93.07% at the concentration of 25% and 50%, respectively. These findings suggest that aqueous extracts of *C. humilis* (obtained by infusion and decoction) could be exploited in the development of natural drugs effective against urinary stones problems.

Antidiabetic activity

The antidiabetic activity of *C. humilis* and *O. oleaster* extracts has been proven through different *in vitro* and *in vivo* studies, whereas no published study has been dedicated to demonstrating the antidiabetic activity of *A. albus* although its ethnomedicinal use in the treatment of diabetes has been documented.

Thus, concerning *C. humilis,* Attaallah *et al.* [29] tested the antidiabetic effect of *C. humilis* extract obtained by infusion using a new electrochemical sensing system (glucometer). This system, a blood glucose reading device, allows the measurement of the enzyme alpha glucosidase (AG)

inhibition by MAPs. The results of this study showed that the aqueous extract of *C. humilis* induced a significant inhibition of AG with a median inhibitory concentration IC_{50} = 5.90 mg/ml. In another study [30], the hypoglycemic and the hypolipidemic effect of *C. humilis* aqueous extract was tested on Meriones shawi rats. In the acute study, the oral administration of a single dose of this extract by experimentally induced hyperglycemia, hyperlipidemia, obese (HHO) rats has led to a significant decrease of their plasma glucose levels (From 12.04 ± 0.94 mmol/l to 6.88 ± 1.38 mmol/l), whereas in the sub-chronic study, the oral administration of *C. humilis* aqueous extract during 30 days by HHO rats resulted in a significant decrease of their weight (from 241 ± 8 to 165 ± 11 g) and plasma glucose levels (from 12.04 ± 0.94 to 4.84 ± 0.22 mmol/l), as well as in total cholesterol (from 3.46 ± 0.21 to 0.62 ± 0.02 mmol/l) and triglycerides (from 1.15 ± 0.17 to 0.37 ± 0.03 mmol/l). These findings support the traditional use of *C. humilis* in the treatment of diabetes and its complications [17,26,63].

As regards *O. oleaster*, Bechiri *et al.* [103] found that aqueous extract of *O. oleaster* leaves exhibited an inhibitory effect on α-amylase with an IC_{50} = 1.23 ± 0.08 mg/ml. Moreover, this extract showed also an *in vivo* antidiabetic effect in starch loading induced diabetic rats, by reducing their postprandial blood glucose level after 180 minutes of starch administration. Similarly, Mezouar *et al.* [93] examined the *in vitro* antidiabetic effect of *O. oleaster* hydromethanolic and hydroacetonic extracts on the inhibition of α-amylase enzyme, and obtained an important antidiabetic effect of the hydromethanolic extract (0.91 ± 0.02 mg/ml) which was higher than that obtained with the hydroacetonic extract (0.54 ± 0.02 mg/ml). In another study, Mechchate *et al.* [44], demonstrated the antidiabetic effect of flavonoids extract of *O. oleaster* leaves. In fact, the studied extract at concentrations of 25 and 50 mg/ml induced an important antidiabetic effect in mice with severe diabetes (<450 mg/dl) resulting from alloxan injection. The investigation of flavonoids chemical profile of the tested extract revealed the presence of different flavonoids responsible for the antidiabetic effect namely amentoflavone, quercetin-3-O-glucoside, quercetin-3-O-hexose-deoxyhexose, luteolin-7-O-glucoside, oleuropein, and rutin. More recently, Kabach *et al.* [39] revealed the antidiabetic effect of *O. oleaster* fruits methanolic extract using *in vitro* assays. Indeed, this extract induced the inhibition of α-amylase and AG enzymes at low concentrations (IC_{50} = 2.367 and 1.272 mg/ml, respectively). This activity could be attributed to the richness of the tested extract in phenolic compounds such as oleoside, ligstroside, and oleuropein glucoside [39].

Neuroprotective activity

Bouhafsoun *et al.* [28] tested using the Ellman method, the effect of methanolic and aqueous extract of *C. humilis* leaves and fruits against two enzymes linked with neurodegenerative diseases, namely acetylcholinesterase (AChe) and butyrylcholinesterase (BChe). The obtained results revealed that all fruits extracts were moderately active against BChe at 200 µg/ml, whereas, they were not active against AChe. Also, no leaves extract was active against the two targeted enzymes. These findings could be explained by the presence of certain active compounds in *C. humilis* fruits extracts that are able to exert an inhibitory effect on BChe enzyme. Thus, further studies are required in order to investigate the different chemical compounds of *C. humilis* methanolic extract and their possible mechanism on BChe enzyme. Similarly, Gonçalves *et al.* [22] studied the inhibitory activity of *C. humilis* methanolic extract obtained from different parts (leaves, seeds, fruit peel, and pulp) against three enzymes: AChe, BChe, and tyrosinase (Tyr) associated with neurodegenerative diseases. The strong inhibitory activity was obtained with seeds and pulp extracts against Tyr (IC_{50} = 268.97 and 279.99 µg ml^{-1}, respectively), as well as with seeds and peel extracts against AChe (IC_{50} = 660.16 and 653.68 µg ml^{-1}, respectively) and against BChe (IC_{50} = 304.86 and 701.54 µg ml^{-1}, respectively). In this study, the enzymes inhibition activity was highly correlated with the total condensed tannins content of the studied extracts. These results suggest that these compounds may be responsible for: Tyr; AChe and BChe inhibitory activity of the extracts which can be used as natural alternative sources of neurodegenerative diseases medical agents.

Antiviral activity

The viral replication and transcription of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (the new strain of Coronavirus) is mediated by a key enzyme: the main protease (MPRO) of SARS-CoV-2. Thus, this enzyme constitutes the main target of SARS-CoV-2 drugs. The inhibitory potential of natural molecules against SARS-CoV-2 MPRO was investigated by Ouassaf *et al.* [31] by molecular and dynamics simulations studies using different softwares (Autodock Vina software and Web server SwissADME). Among 50 molecules of several medicinal plants; kaempferol and Tricin-7-O-neohesperidoside which are secondary metabolites of *C. humilis* [21,76] displayed suitable molecular properties for SARS-CoV-2 MPRO inhibition. These results are promising for the development of natural drugs against SARS-CoV-2 from *C. humilis* chemical compounds.

In another study, Ben-Amor *et al.* [41] demonstrated the antiviral activity of *O. oleaster* leaves hydroethanolic extract against herpes simplex virus type 1). In fact, this extract induced an important selective effect against pre-infection and post-infection of Vero cells without inducing a cytotoxic impact on these cells. This effect could be related to the presence of several phenolic compounds such as Oleuropein hexoside, Oleanolic acid, and Epicatechin [41].

Hepatoprotective

The hepatoprotective activity of some extracts of *O. oleaster* and *A. albus* has been demonstrated. Thus, Al-Attar *et al.* [43] assessed the hepatoprotective effect of *O. oleaster* leaves aqueous extract in albino mice. They found that this extract reduced significantly hepatocirrosis resulting from thioacetamide administration by the tested animals. Indeed, histopathological observations revealed the attenuation of structural damage in mice liver after their treatment with the extract. Serairi-Beji *et al.* [52] studied the hepatoprotective activity of *A. albus* leaves aqueous extract in male waster rats intoxicated with Tetrachloromethane. The results showed

that this extract exerted a high protective activity by reducing levels of enzymes hepatic markers (lactate and aspartate transaminases), and by preventing the histological structure of rats liver from damage. The hepatoprotective effect of this extract could be related to its richness in phenolic compounds such as gallic acid, catechin, rutin, and quercetin [52].

Antihyperlipidemic

Olea oleaster oil has been revealed to play an important role in the modulation of plasma lipids. Thus, Belarbi *et al.* [11] demonstrated the effect of *O. oleaster* oil on the modulation of plasma lipîds in human. Indeed, after 1 month of *O. oleaste*r oil administration by 40 healthy Algerian human subjects, a significant attenuation of their total cholesterol, low-density lipoprotein cholesterol, and plasma triglyceride concentration was recorded, in comparison with non-consuming people originating from the same area.

Cytotoxic activity

The cytotoxic activity of different *O. oleaster* extracts has been proven. Thus, Makowska-Wąs *et al.* [40] studied the cytotoxic activity of *O. oleaster* leaves methanolic extract against human normal (prostate epithelial (PNT2), skin fibroblasts (BJ)) and cancer cells (hepatocellular carcinoma (Hep G2)), prostate cancer (DU-145 and PC-3), and melanoma (HTB-140 and WM793). For this study, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay was performed. The results showed that the tested extract exhibited an important cytotoxic activity against prostate cancer cells and had less effect on the viability of liver cancer cells, whereas it did not impact the viability of melanoma and normal cells. These results may be exploited in the development of new drugs from *O. oleaster* leaves extracts against prostate cancer. However, further *in vivo* studies are definitely needed. Furthermore, it is important to mention that the cytotoxic activity of *O. oleaster* leaves methanolic extract is probably related to its richness in bioactive compounds, including phenolic acids and the major polyphenol compound (Oleuropein) [40]. In another study, Zeriouh *et al.* [104] demonstrated that *O. oleaster* aqueous extract limited human colon cancer (HCT116) xenograft growth in mice, and induced cellular apoptosis of two colorectal cell lines (HCT116 and HCT8) through the activation of caspase enzymes. Furthermore, Ghorbel *et al.* [85] revealed the autophagic activity of *O. oleaster* fruits EAFs in human foreskin fibroblasts. This activity of the tested extract could be exploited in cancer treatment, since autophagy is becoming nowadays an essential approach in tumors suppression and in cancer management. Recently, Kabach *et al.* [39] investigated the cytotoxic effect of *O. oleaster* fruits methanolic extract against two cell lines of human breast cancer (MCF-7 and MDA-MB-468) using the same assay. They obtained an important cytotoxic activity for the studied extract with a median anti-proliferative inhibitory concentration of 46.75 and 35.16 µg/ml against MCF-7 and MDA-MB-468, respectively. The demonstrated cytotoxic activity could be attributed to the presence of several bioactive compounds in the extract such as rutin, oleuropein, and verbascoside [39], which were demonstrated to possess a high cytotoxic effect [103,105-107].

CONCLUSION

This review shows that *C. humilis, O. oleaster,* and *A. albus* are interesting medicinal plant species that can be used not only in the medical field for human therapy, but also in the food industry and agricultural sectors. Indeed, different ethnobotanical studies have revealed the traditional use of these Mediterranean plants for the treatment of several ailments. Moreover, numerous scientific works conducted either *in vitro* or *in vivo* on animal models have shown the multiple biological activities of *C. humilis* and *O. oleaster,* including their antioxidant, antimicrobial, antidiabetic, and antiviral properties. However, in the case of *A. albus,* there is a lack of experimental studies on its biological activities. Thus, further studies are required in this context. Furthermore, the bioactive potential of these three Mediterranean plant species was attributed in several studies to their richness in bioactive compounds belonging to different chemical classes, such as flavonoids and phenolic acids which are abundant in the three plant species, and other compounds like oleuropein; a secoiridoid present only in *O. oleaster*. In addition, it is important to mention that it is extremely interesting to exploit the therapeutical potential of the studied Mediterranean plants in the development of natural drugs. Moreover, the antimicrobial and antioxidant properties of these plant species are encouraging their use in the food industry and agricultural sector as green additives and bio-pesticides replacing the chemical products used in these fields.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the international committee of medical journal editors (ICMJE) requirements/guidelines.

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CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

DATA AVAILABILITY

All data generated and analyzed are included in this article.

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USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declares that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript, and no images were manipulated using AI.

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