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Review

Lentisk fruits (*Pistacia lentiscus* L.) as sources of phytochemicals with potential health benefits: A review

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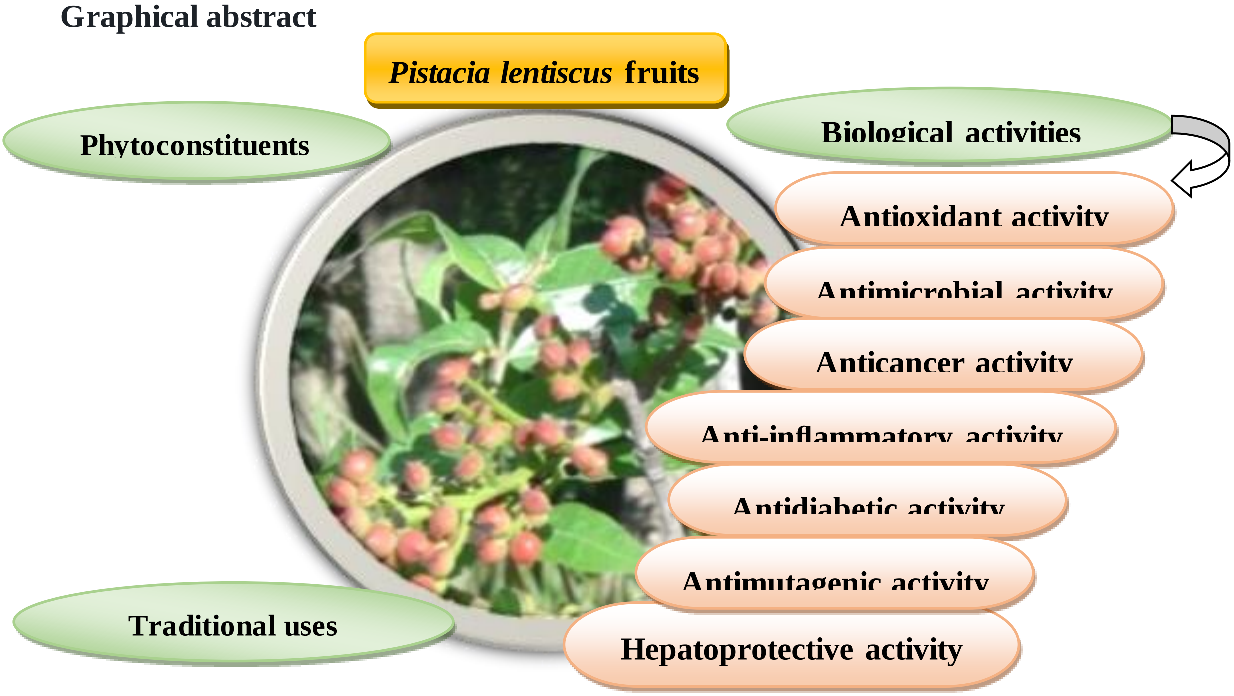
Highlights

- *Pistacia lentiscus* L. is a medicinal aromatic plant belonging to the Anacardiaceae family.
- *P. lentiscus* fruits are rich in phenolic acids, tannins, flavonoids, sterols, triterpenes, anthocyanins, and alkaloids.
- It is an herbal medicine that treat some diseases (respiratory problems, digestive system, etc.)
- *P. lentiscus* fruits revealed antioxidant, antimicrobial, anticancer, anti-inflammatory, antidiabetic, antimutagenic, and hepatoprotective activities.

Graphical abstract



Abstract

The field of phytochemistry is increasingly interested in the use of plants in order to discover new therapeutic treatments, by scientifically proving their role, as popular remedies against diseases. *Pistacia lentiscus* L. is a medicinal and aromatic plant belonging to the Anacardiaceae family. The distribution of this plant includes Mediterranean area. Indeed, it is very used in Algerian traditional medicine.

Different parts of this specie have been used in traditional medicine to treat some diseases, such as respiratory problems, disorders of the digestive system, hypertension, coughs, sore throats, eczema, stomachaches, kidney stones and jaundice in many countries.

Scientific findings also revealed the wide pharmacological activities from various parts of this specie, such as antioxidant, anti-inflammatory, antimicrobial, antiviral, antimutagenic, antidiabetic, hepatoprotective and anticancer activities. Many phytochemical constituents like phenolic compounds, terpenoids, fatty acids, and sterols have also been extracted and identified from different parts of *Pistacia* species in many recent studies.

The objective of this review was to screen the biological properties of *P. lentiscus* extracts and oils of fruits. Starting from this, we had first researched the phytochemistry composition of this part collected from different geographical areas and then reported the traditional uses. In the second part, we had presented the scientific discovery of its potential and biological activities.

Keywords: *Pistacia lentiscus.* L; Traditional medicine; Phytochemistry; Biological activities.

Abbreviations

EO: Essential oil; **RD cells:** Rhabdomyosarcoma cells; **COX/-LOX** (cyclooxygenase/-lipoxygenase); **IL-1β**: interleukin 1 bêta; **Wt., p.o:** weight- toxicity., oral taken; **Wt., I,p:** weight- toxicity., intraperinal taken; **CAT:** Catalase; **SOD:** Superoxid dismutase; **AOPP:** advanced oxidation protein products**; MDA:** Malondialdehides; **GP$_X$:** Glutathione peroxidase; **PlL:** *Pistachia lentiscus* L.

1.Introduction

Recently, natural compounds isolated from aromatic and medicinal plants are of great pharmaceutical interest due to their potent biological properties (Elloumi et al., 2022).

Pistacia lentiscus L belongs to the Anacardiaceae family, an evergreen tree widely distributed in the Mediterranean region. This specie includes about 70 genera and over 600 species (Ierapetritis et al., 2010). This specie is well known for its health promoting effects attributed to its composition comprising essential oil, fatty acids and polyphenols (Dahmoune et al., 2014; Garofulic et al., 2020). Recent studies have shown that all parts of *P. lentiscus* were rich in phenolic acids and flavonoids, mainly represented by hydroxybenzoic acids and flavonols (Belhachat et al., 2017). These compounds have a wide range of positive biological effects. Several scientific studies have proven that they are responsible for the antioxidant activity of P. lentiscus, thanks to their redox properties, which allow them to be used as reducing agents, metal chelators and simple oxygen quenchers and hydrogen donors (Pilluza et al., 2011). In addition, further interesting capabilities have been ascribed to these phytochemical compounds with strong antimicrobial, anti-inflammatory, antioxidant properties and other pharmacological effects. Also, the high level of polyphenols found in the extracts gives them a capacity to fight against chronic and degenerative diseases (Milia et al., 2021).

The aim of the present work was to give an overview of the traditional uses of *P. lentiscus* and beneficial effects of its fruit’s extracts and oils, expanding the search for the scientific discovery of their chemistry, potential and biological activities.

2. Botanic description

Lentisk (*P.lentiscus*), commonly called "Dro" in the local Arabic, is a branched shrub three meters high, with a strongly acrid resin smell (figure 1). It is a species of the Anacardiaceae family, dioecious evergreen. The flowers are in dense spike-like clusters, reddish in color, unisexual and very aromatic. The fruit of the pistachio tree is a globose berry of 2 to 3 mm monosperm; first red, then black when ripe (Amara et al., 2019).

Pistachio is a thermophilous evergreen shrub growing wild in a wide range of habitats throughout the Mediterranean countries and Canary Islands. It is abundant in sunny scrublands of Eastern and Southern Iberian Peninsula, sharing their habitats with species, such as *Chamaerops humilis* L., *Quercus coccifera* L., *Rhamnus lycioides* L., etc. It can adapt a varied range of substrates (Llorens-Molina et al., 2015). What's more, it develops in several Mediterranean regions, and is generally dispersed in Algeria all along the coast.

The environment of the plant, related to geographic sources, climatic and meteorological conditions, nature of the soil, harvest time during the day, sunshine, harvesting seasons, neighboring plant populations may influence the chemical composition of the plant (Selmi et al., 2020).

According to many studies, recent data carried out in different Mediterranean countries show a wide range of chemical variability affecting both major compounds and total amounts of terpene classes, monoterpene hydrocarbons represent the major fraction, mainly in ripe fruits (96.3 – 98.8 %) and in fresh or dried leaves and twigs (20.0 – 75.8 %). Nevertheless, strong variability can be observed according to the harvest time and the place of sampling, even when it is carried out in close locations in the same country. Indeed, samples containing up to 82.69 % of sesquiterpene fraction have been reported and oxygen-containing monoterpenes in leaves fluctuate between 0.97 % and 55.0 %. Small amounts of diterpenes (dimyrcene isomers) have also been reported (0.47 %, 0.53 %, 0.81 % in leaves, unripe and ripe fruits, respectively) and (0.16 % in twigs). This strong chemical variability agrees with the high degree of morphological and physiological plasticity related to its environmental tolerance and therefore, its wide range of habitats in which it grows (Llorens-Molina et al., 2015). The chemical composition of the essential oil derived from the aerial parts is not clear. It is greatly influenced by both geographical origin and isolation technique (Amhamdi et al., 2009).

Figure 1. *Pistacia lentiscus* L.

3. Phytochemical Constituents

P. lentiscus is a wild-growing shrub rich in terpenoids and polyphenols (Quartu et al., 2012). Fruits are used for preparations of EO and also alcoholic extracts. Hydro-distillation using Clevenger-type devices has been the more common method to obtain the oil from fruits. However, the oil obtained by hydro-distillation and the extracts by solvents can have different organoleptic profiles and chemical compositions. Various compounds from different phytochemical groups were identified in *P. lentiscus* fruits. The major ones are summarized below in the Table1.

3.1. Terpenes and terpenoids

One of the main components reported from fruits is the essential oil. Its analysis is mostly performed by means of gas- chromatography (GC) based technic. There are many qualitative and quantitative variations between the content of essential oils which are related to several parameters like plant species and part, harvesting time, geographical origin, sex of cultivars, and climatic conditions (Alma et al., 2004 ; Benamar et al., 2010).

The essential oil is constituted by a mixture of terpenes and terpenoids, mainly monoterpenes and sesquiterpenes, which are also responsible for the characteristic smell and the flavoring of the plant (Inbar et al., 2004; Loi et al., 2002; Melia et al., 2021; Quartu et al., 2012). Up to 64 chemical constituents have been reported in the PlL EO fingerprint, in addition to other fractions that cannot be quantified by the assays (Melia et al., 2021). α-pinene and limonene are the main components in fruit essential oil (Bouyahya et al., 2019).

The phytochemical screening of fruits showed the great presence of sterols, triterpenes, oses, holosides, reducing sugars, mucilages, and alkaloids (Barbouchi et al., 2020). The major chemical constituents in EO are hydrocarbon and oxygenated monoterpens (Fernandez et al., 2000; Koutsoudaki et al., 2005). β-myrcene (54%), α-pinene (22%) in unrip fruits and β-myrcene (19%), α-pinene (11%), δ-3-carene in rip fruits **(**Boelens and Jiminez, 1991). Monoterpens are also detected in mastic water which was separated from the mastic oil during steam distillation**.** Phenolic composition of seed oil is also detected in rip oil fruits (Mezni et al., 2015). α-pinene (13.35%), α-phellandrene (10.12%), β-phellandrene (10.45%), sabinene (7.01%), germacrene-D (6.86%), β-caryophyllene (4.58%) are also detected in fruits **(**Ben Khedir et al., 2016). 4-{3-[(2hydroxybenzoyl) amino] anilino}4-oxobut-2-enoic acid (28.96%), β-myrcene (11.47%), 3-pentadecylphenol (8.51%), p-tolyl ester (8.36%), amino formic acid (7.51%) in fruits **(**Ammari et al., 2018). β-myrcene (75.6%), α-pinene (12.6%), α-limonene (3.2%), α-terpineol (1.4%), camphene (0.8%) in ripe fruits.

3.2. Phenolic Compounds

Phytochemical screening showed the presence of phenolic compounds, flavonoids, antocyanins, leucanthocyanins, phlobotannins, tannins, saponins, terpenoids, proteins and mucilage with absence of alkaloids, quinones and carotenoids (Belhachat et al., 2017). Fruits from different areas were rich in anthocyanins, condensed tannins, Gallic tannins and flavonoids. While they were free of saponosides and alkaloids (Boudieb et al., 2019). Milia et al. (2021) has illustrated total phenolic acids 436.4–2762.7 mg/kg; total flavones 75.3–1222.9 mg/kg; total flavonols 24.2–377.4 mg/kg; total secoiridoids 12.6–366.8 mg/kg; total phenols 538.0–4260.6 mg/kg from methanol/water fruit extract. Several studies have confirmed that the *Pistacia lentiscus L.* plant is rich in phenolic compounds (Bampouli et al., 2014; Zitouni et al., 2016; Barbouchi et al., 2020).

Six phenolic compounds for gallic acid, catechin, 3,4-dihydroxyhydro-cinnamic acid, benzoic acid, salicylic acid, and luteolin were identified in fruits. The presence of gallic acid and quercetin-3-O-rhamnoside in the leaves of *P. lentiscus* was previously reported (Mehenni et al., 2016). Gallic acid, constitutes the basic unit of galloyl tannins and is a hallmark of *Pistacia* species. Bhouri et al. (2010) demonstrated that fruits contain digallic acid, 1,2,3,4,6-Pentagalloyl glucose and gallic acid compounds. Flavonoid compounds have been also detected in fruits.

Trabelsi1 et al. (2016) has identified high levels in flavonoïds (from 13.78 mg RE/ g dw (RM) to 23.46 mg RE/ g dw (TB)) and in total phenolic compounds (from 24.84 mg GAE / g dw (KO) to 46.07 mg GAE/ g dw). The main polyphenols are phydroxybenzoic acid, gallic acid, cinnamylidene acetic acid, quinic acid, p-coumaric acid 4-O-glucoside, 5-galloylquinic acid, isomer of caffeoylquinic acid, 3,4,5 O-trigalloylquinic acid, quercetin, taxifolin, quercetin-3-Oglucuronide, luteolin 6,8-di-C-hexoside, oleoside and epirosmanol.

Table 1. Chemical composition of *P. lentiscus* L. fruits.

Compound-family	Chemical family	Examples of some molecules
Terpenoids	***Monoterpene Hydrocarbons***	α-pinene (Mecherara-Idjeri et al., 2008 ; Bouyahya et al., 2019) ; β-myrcene (Benyoussef et al., 2005 ; Castola et al., 2000 ; Congiu et al., 2002) ; Limonene (Roitman et al., 2011; Bouyahya et al., 2019) ; δ-3-carene (Boelens and Jimenez, 1991; Milea et al., 2021); Camphene (Boelens and Jimenez, 1991; Milea et al., 2021).
	Sesquiterpenes	b-caryophyllene ou α-humulene and ε-cadinene (Boelens and Jimenez, 1991).
Phenolic compounds	***Total phenolic acids*** *436.4–2762.7* mg/kg	Gallic acid (Abdelwahed et al., 2007); Digallic acid (Bhouri et al., 2010); phydroxybenzoic acid, gallic acid, cinnamylidene acetic acid, quinic acid, p-coumaric acid 4-O-glucoside, 5-galloylquinic acid, isomer of caffeoylquinic acid, 3,4,5 O-trigalloylquinic acid (Trabelsi et al., 2016).
	Aromatic acids	Hydroxycinnamates from (5.4±0.2) to (22.2±0.8) mg/g as caffeic acid equivalent in methanol extract (Botsaris et al., 2015).
	Flavonoids: 16.57 ± 1.11 mg E R/g (Mehenni et al., 2016).	Catechin (flavonol) 0.2 ± 0.001 mg/ g, and Luteolin (flavone) 2.97 ± 0.1 mg/g (Mehenni et al., 2016). Quercetin, Taxifolin (dihydroquercetin), Quercetin-3-O-glucuronide, and Luteolin 6,8-di-C-hexoside (Trabelsi et al., 2016).
	Tannins: 309.45 ± 6.88 mg TA Eq/g (Mehenni et al., 2016).	1,2,3,4,6-Pentagalloyl glucose (Abdelwahed et al., 2007).
Lipid content about 42.54%	***Oils, fatty acids***	Monounsaturated fatty acids: Palmitoleic acid (C16:1 n-7), Oleic acid (C18:1 n-9) Gondoic acid (C20:1 n-9), Palmitelaidic acid (C16:1 n-9), Vaccenic acid (C18:1 n-7), Paullinic acid (C20:1 n-7), Erucic acid (C22:1 n-9) (Brahmi et al., 2020). Polyunsatured acids: Linoleic acid (C18:2 n-6), Linolenic acid (C18:3 n-3), Eicosadienoic acid (C20:2 n-6) Satured acids: Palmitic acid (C16:0), Stearic acid (C18:0), Arachidic acid (C20:0) (Trabelsi et al., 2012 ; Brahmi et al., 2020) ; Lauric acid (C12:0), Tridecylic acid (C13:0), Myristic acid (C14:0), Pentadecylic acid (C15:0), Margaric acid (C17:0), Heneicosylic acid (C21:0), Behenic acid (C22:0), Tricosylic acid (C23:0), Lignoceric acid (C24:0), Pentacosylic acid (C25:0), Cerotic acid (C26:0) (Brahmi et al., 2020).
	Sterols	b-Sitosterol the major 4-desmethylsterol followed by Campesterol. Cholesterol and Stigmasterol were detected in trace amounts. The content of sterol is from

5.19/100 g to 0.43/100 g of oil (Trabelsi et al., 2012).

3.3. Fatty acids and sterols

Others compounds like oils, fatty acids and sterols have been illustrated from fruits during maturation in petroleum ether extract (Milia et al., 2021).

P. lentiscus can be regarded as an oleaginous plant. The oil content in fruits has been estimated from 1.83 to 42.54 % of dried weight (Trabelsi et al., 2012; Yousi et al., 2002).

4. Traditional uses of *P. lentiscus*

The effectiveness and reliability of medicinal and aromatic plants have been confirmed by their beneficial therapeutic effects, in traditional folk medicine. Recently, research works have confirmed that natural metabolites of plants are very interesting compounds for alternative remedies for various diseases. According to the World Health Organization (WHO), nearly 65% of the world's population has integrated plants and traditional medicine as an additional modality of health care (Kazemi et al., 2012; Sharif et al., 2012).

P. lentiscus has a long tradition in ancient medicine (Table 2). However, all parts of the plant, including leaves, fruits, roots and stems have been used in folk medicine since ancient times, due to their health benefit effects (Elloumi et al., 2022). In Algeria, aerial parts of this plant have traditionally been used in the treatment of the stomachaches, hypertension, sore throats coughs, eczema, kidney stones and jaundice, and also for possess stimulant and diuretic properties (Amhamdi et al., 2009; Saiah et al., 2016).

The ethnobotanical survey by Boudieb et al. (2019) showed that all products of *P. lentiscus* from Algeria were consumed mainly for the treatment of certain types of diseases, such as respiratory problems and disorders of the digestive system. These results are in agreement with those found by other studies reported by Bammou et al. (2015) and Hafsé et al. (2015). In north Africa, this specie is used i the treatment of hypertension, cardiac diseases and diabetes (Lepprotti et al., 2009 ; Trabelsi et al., 2012 ; Fakchich and Lachouri, 2014). Similar beneficial effects have been reported by using the plants growing in the spain and Italy (Benitez et al., 2012; Gras et al., 2019). According to Giner-Larza (2001), *P. lentisus* from Turkey is used traditionally to treat throat infections, asthma, eczema, stomach ache, renal stones, paralysis, diarrhea, jaundice, antimicrobial, anti-inflammatory, antipyretic, astringent and stimulant. In Iran, this plant has been largely used as a remedy against Gum tissue strengthened, breath deodorizer, brain and liver tonic and gastrointestinal ailments (Rahimi et al., 2009 ; Farzaei et al., 2013).

P. lentisus has been considered as one of most used plants in Sardinia s' traditional pharmacology. It has been emerged as a therapeutic agent against inflammation and infection of the oral cavity, osteoarthritis, bronchitis, cough sedative, antipyretic, allergies, asthma, ulcerations, gastrointestinal disorders, wound healing and haemostatic (Barra et al., 2007 ; Di Rosa, 2018 ; Loi et al., 2002; Sachetti et al., 2001).

Table 2. Traditional and ethnopharmacological uses of *P. lentiscus*.

Geographical Area	Traditional uses	Reference
Algeria and North Africa	hypertension, coughs, sore throats, eczema, stomach aches, kidney stones, jaundice, stimulant and diuretic properties, respiratory problems, disorders of the digestive system.	Amhamdi et al. (2009) ; Saiah et al. (2016) ; Boudieb et al. (2019) ; Bammou et al. (2015) ; Hafsé et al. (2015).
	Hypertension, cardiac diseases and diabetes.	Lepprotti et al. (2009) ; Trabelsi et al. (2012) ; Fakchich and Lachouri, (2014).
Italy and Spain	Hypertension, cardiac diseases and diabetes.	Benitez et al. (2012) ; Gras et al. (2019).
Turkey	Throat infections, asthma, eczema, stomach ache, renal stones, paralysis, diarrhea, jaundice, stimulant and astringent.	Giner-Larza (2001).
Iran	Gum tissue strengthened, breath deodorizer, brain and liver tonic and gastrointestinal ailments.	Rahimi et al. (2009) ; Farzaei et al. (2013).
Sardinia	Inflammation and infection of Oral cavity, osteoarthritis, bronchitis, cough sedative, antipyretic effect, allergies, asthma, ulcerations, and gastrointestinal disorders.	Barra et al. (2007) ; Sachetti et al. (2001) ; Di Rosa (2018) ; Loi et al. (2002).

5. Potential and biological activities of *P. lentiscus* fruits

5.1. Fruits of *P. lentiscus* in nutrition

The fruits can be used rawly or roasted, while their oil can be used traditionally as an internal treatment for ulcers or externally for the treatment of some skin diseases like psoriasis (Benhamou et al., 2008). The results of the same authors proved the richness of this oil in unsaturated fatty acids (70%) and saturated fatty acids (26%), which makes it of good nutritional quality. Other parts of *P. lentiscus* have also used in the food industry. For example, the essential oils obtained from the aerial parts have used as flavouring agents in chewing gums and alcoholic drinks (Zrira et al., 2003). In addition, the anthocyanins extracted from the fruit are used as food colorants. Moreover, a large amount of phytosterols such as β- sitosterol, vitamins and oil rich in monounsaturated and omega-3 fatty acids such as oleic acid and linolenic acid can eventually be incorporated into animal and human diets as antioxidants (Bozorgi et al., 2013).

5.2. Antioxidant Activity

Several recent studies have proven that *P. lentiscus* fruits have been shown *in vitro* radical scavenging properties. As reported by Belhachat et al. (2017), the berries ethanolic extract possessed strong scavenging activity against DPPH·, $ABTS^{\cdot+}$ free radical scavenging activity and reducing power. Same tests were used by Djebari et al. (2021), who reported that fruits macerate showed high antioxidant capacity by DPPH (%), ABTS and FRAP (fruits IC_{50} = 193.48 ± 3.16 µg/ mL for DPPH, 155.92 ± 1.09 µg for ABTS and 55.54 ± 1.41 µg/ mL for FRAP). Barbouchi et al. (2020) and Arab et al. (2015) indicated that fruits and all other parts of *P. lentiscus* could be taken as a potential natural source of antioxidants, and may have a great interesting as a natural antioxidant able to prevent oxidative stress.

Besides, Hemma et al. (2018) revealed that the methanolic extracts of fruits contain high levels of phenolic compounds. The test of antioxidant activity showed a strong reducing activity of fruits methanolic extract, with a high percentage of reduction which were superior than 73% with an EC_{50} (0,26 mg/ ml ± 0.0002) for fruits in the free radical DPPH test. Morever, the Ferric Reducing antioxidant power assay FRAP revealed a high reduction power proportionally to the concentration of the extract.

Moreover, in the study reported by Mehenni et al. (2016), the antioxidant properties of *P. lentiscus* were determined by the oxygen consumption method. According to results of this investigation, *P. lentiscus* fruits extract reduced the rate of oxygen consumption by 11%, less than that of catechin (76%), but in agreement with previous results confirmed by Diouf et al. (2006), and Eidi et al. (2012).

The antioxidant activity of *P. lentiscus* extracts was estimated by *in vitro* assays in the study of Botsaris et al. (2015). The DPPH radical scavenging activity in fruits was from (70.2±5.3), while the ABTS radical scavenging activity ranged from (21.3±7.3) to (290.2±28.1) mg per g of extract in fruits. In FRAP assay, a great diversity of antioxidant activities was found among the extracts (from (42.2±2.4) to (518.8± 37.2) mg of TE per g of extract).

Antioxidant activity has been also reported from oils of fruits; the results of Belyagoubi Benhammou et al. (2018) showed that fatty oil of fruits has a height capacity to scavenge DPPH radical (EC_{50} = 20.619 ± 0.312 mg/mL).

Furthermore, the antioxidant activity of *P. lentiscus* fruits essential oils showed interesting antioxidant effects than *P. lentiscus* leaves essential oils by an antioxidant capacity values of IC_{50} = 29.64 ± 3.04 µg/mL, IC_{50} = 38.57 ± 4.22 µg/mL, and IC_{50} = 73.80 ± 3.96 µg/mL revealed by DPPH, FRAP, and ABTS assay, respectively. In the light of the results obtained, it appears that the essential oil of fruits is rich in substances having a powerful antioxidant power Bouyahya et al. (2019).

In addition, the results of Aouinti et al. (2014) revealed that *P.lentiscus* L. oil has a power antioxidant activity against DPPH·.

The results thus discussed confirm that this species is a promising source of new natural antioxidants.

5.3. Anticancer activity

The anticancer effect was investigated in the study of Bouyahya et al. (2019) on RD and L20b adenocarcinoma cancerous cell lines. *P. lentiscus* fruits essential oils showed remarkable cytotoxic effects these cells lines at IC_{50} values of 26.43 ± 2.18 µg/mL and 33.02 ± 2.84 µg/mL, respectively. In the contrary, Yemmen et al. (2017) showed that the leaf extract exhibited an important antiproliferative activity (IC_{50}: 135.67 ± 2.5 and 250.45 ± 1.96 µg/ml in CaCo2 and AGS cells respectively) but the infusion extracts of fruit was inactive.

5.4. Antimicrobial activity

Several studies reported the antimicrobial activity of *P. lentisus* oils and extracts, trying to clarify scientifically their popular use against infectious diseases.

According to the results of Carrol et al. (2020), the ethanol extract of fruits indicated the most high inhibition potential against *Porphyromonas gingivalis* in comparison to 20 other extracts of pharmaceutical plants. On the other hand, the potency of the fruits extract was higher than that of the leaves and woody parts, with MIC values against *P. gingivalis* of 8 µg/mL.

In the study of Djebari et al. (2021), the evaluation of the antibacterial activity related to different macerates of *P. lentiscus* was studied with respect to 9 bacterial strains chosen for their high frequency to induce food-borne and gastrointestinal infection. Macerate fruits showed the largest diameter of inhibition in case of *Staphylococcus epidermidis* (9.50 ± 0.5 mm) and *Bacillus subtilis* (10.50 ± 1.50 mm).

Similarly, Mandrone et al. (2019) confirmed through their study that the antimicrobial activity of MeOH aqueous extracts of fruits and leaves has been related to the concentration of phenolic components. This is due to the activity of phenols against multidrug resistant bacteria, namely MRSA and carbapenemase producing Klebsiella pneumoniae. According to Milia et al. (2020), Low or no susceptibility of the yeasts to the leaves extract, or to the fruits oil, was detected concerning *Candida spp*. Furthermore, *P. lentiscus* leaves essential oil from Sardinia had low MIC values against *C. glabrata* and *C. albicans*. In addition, the results of Liu et al. (2016) were attributed to the recurrence of pharmacological concentrations of six terpenes, which were greater than 0.05% in the imprint. In this study, also, the essential oil demonstrated its ability to inhibit COX-2 and LOX, which are proteins that are highly conducive to Candida virulence.

In study of Mezni et al. (2015), the antimicrobial activity was evaluated using disc diffusion assay and the broth dilution method in both oil and extract of *P. lentiscus* oils were most efficient ($p < 0.003$) against, respectively, *Staphylococcus aureus* and *Aspergillus niger* with an inhibition zone of 9.33 mm. The phenolic extract showed the largest spectrum of sensitive microorganisms. The minimum inhibitory concentration and minimum bactericidal concentration results revealed that all strains were inhibited by both. According to results of Benhamou et al. (2008), extracts of the phenolic compounds of *P. lentiscus* showed power antimicrobial activity.

5.5. Antimutagenic Activity

The studies reported by Bhouri et al. (2010) and Abdelwahed et al. (2007) confirmed that gallic acid, digallic acid, and 1,2,3,4,6-pentagalloylglucose, polyphenols isolated from the fruits of *P. lentiscus*, exhibited an inhibitory activity against mutagenicity and genotoxicity in in vitro tests.

5.6. Antidiabetic activity

P. lentiscus fruits extract induced a promising antidiabetic activity in streptozotocin-induced diabetic rats, similar to the reference drug glibenclamide (0.91 g/L). The result was attributed *in vitro,* by the inhibition of a-amylase (Mehenni et al., 2016).

5.7. Hepatoprotective activity

In the study realized by Mehenni et al. (2016), hepatoprotective potential against paracetamol [165 mg/kg body weight (b.w.)] toxicity was noticed in mice pretreated with the same dose of *P. lentiscus* fruits extract (125 mg/kg b.w.) as revealed by an analysis of biochemical parameters (alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase activities and total bilirubin). These results were confirmed by histological examination of the liver, which exhibited significant protection against paracetamol-induced hepatic necrosis.

5.8. Anti-inflammatory Activity

Remila et al. (2015) tested the anti-inflammatory activity of leaves and fruits extracts by measuring the secretion of IL-1β by macrophages exposed to adenosin triphosphate (ATP) or H_2O_2. Results of this investigation confirmed that *P. lentiscus* leaves extract significantly reduced the production of IL-1β from ATP- or H_2O_2-activated cells. The inhibitory capacity of the leaves extract was higher than fruits and of quercetin and gallic acid (tested as isolated fractions of the polyphenol mixture). According to these authors, this is due to the higher content of total phenols and flavonoids in the leaves compared to the fruits and to the synergy between the pharmacological biomolecules of the extract of *P. lentiscus*. In the work reported by Benkhedir et al. (2016), carrageenan-induced paw edema rat model was used to determine topical anti-inflammatory effect of *P.lentiscus* fruit oil. The topical anti-inflammatory activity was compared to Inflocine and estimated by measuring the diameter of paw edema, for 5 hours at a 1-hour interval. After that, the rats were scarified and the inflamed paw tissue was removed for the exploration of some parameters of oxidative stress and histopathology. *P.lentiscus* fruit oil showed a significant antiinflammatory activity in comparison with the Inflocine. The percentages of edema inhibition were 70% and % 51.5% ($p < 0.01$), respectively, after five hours. The treatment with *P.lentiscus* fruits oil, and Inflocine led to significant increases ($p \leq 0.05$) in the activities of CAT, SOD, and GPX and significant decreases in the MDA level and AOPP activity in the paw tissue after Carragenin injection, compared to the Carr group.

5.9. Others

5.9.1. The healing effect of P. lentiscus fruit oil on laser burn

The study reported by Ben Khedir et al. (2017) showed, for the first time, the healing effect of *P. lentiscus* fruits oil on CO_2 laser fractional burn. The results exhibited that after eight days, the higher percentage of wound healing contraction was observed among the fruits oil -treated group (100%) followed by the 'CYTOL BASIC' treated group (61.36%) and untreated group (32.27%). During the treatment, the fruits oil -treated group revealed less erythema, less crusting/scabbing, higher general wound appearance scores and a high content of collagen (220.67 ± 7.48 mg/g of tissue) than the other groups. Their antioxidant, antimicrobial and anti-inflammatory effects may be the main cause of their wound healing power.

5.9.2. Dermal Wound Healing Effect

The study of Boulebda et al (2009) was realized to determine the effect of *P. lentiscus* fruits fatty oil on cutaneous wound healing in rat. Results substantiated the healing potential effect on wound of a topic application of the *P. lentiscus* fruits fatty oil and its unsaponifiable fraction.

5.9.3. In vitro inhibitory effects on pancreatic lipase, a-amylase, and a-glucosidase

In the investigation of Foddai et al. (2015), fruits aqueous extracts were identified as *in vitro* potent and efficacious dual inhibitors of on metabolic enzymes: Pancreatic lipase a-amylase and a-glucosidase (IC_{50} : 1.4 ± 0.2 mg/mL), and as functional foods and nutraceuticals modulating gastrointestinal carbohydrate and lipid digestion and absorption, may be considered as potential candidate for obesity-diabetes prevention and phytotherapy.

5.9.4. Acute toxicity of P. lentiscus seed oils in mice

The study of Boukeloua et al. (2012) exhibited a low toxicity of *P. lentiscus* seeds fixed oil. The high Mortality percentage or LD_{50} (Lethal dose of 50 % of animals) value in *P. lentiscus* treated mice with oral or intraperineal single dose has been introduced: LD_{50} = 37 ml/kg body wt., p.o.; LD_{50} = 2.52 ml/kg body wt., i.p.). All doses contradiction, orally and intraperitoneally administered, caused immediate agitation and behavioral perturbations with temporary writhing, followed by a quiet attitude period and sedation. Generally, diarrhea was noted and the animals died 12 hours after the administration of fixed oil. Autopsied dead animals showed congested lungs and hearts stopped in diastole. The surviving animals quickly recovered their normal activity and growth, after a period ranging from 4 to 8 days, depending on the dose and mode of administration.

Table 3. Summary of biological activities of *P. lentiscus*.

Biological activities	Fruits extract	Model/ Method	Finding/ Results	Reference
Antioxidant activity	Ethanolic extract	DPPH·, $ABTS^{·+}$, FRAP	Strong scavenging activity	Belhachat et al. (2017) ; Barbouchi et al. (2020) ; Hemma et al. (2018)
	methanolic extract	DPPH·, $ABTS^{·+}$, FRAP	DPPH (70.2±5.3) ABTS radical ranged from (21.3±7.3) to (290.2±28.1) mg of TE per g of extract in fruits. FRAP assay (from (42.2±2.4) to (518.8± 37.2) mg of TE per g of extract).	Botsaris et al. (2015)
	Extract	Oxygen consumption method.	Reduction of oxygen consumption = 11%.	Mehenni et al. (2016), Eidi et al. (2012)
	Fatty oil	DPPH test	hight capacity to scavenge DPPH (EC_{50} = 20.619 ± 0.312 mg/mL).	Benhamou et al. (2018)
	Essential oil	DPPH·, ($ABTS^{·+}$), FRAP	IC_{50} = 29.64 ± 3.04 µg/mL, IC_{50} = 38.57 ± 4.22 µg/mL, IC_{50} = 73.80 ± 3.96 µg/mL revealed by DPPH, FRAP, and ABTS assay respectively.	Bouyahya et al. (2019)
Anticancer activity	Essential oil	RD and L20b adenocarcinoma cancerous cell lines.	remarkable cytotoxic effects on RD (26.43 ± 2.18 µg/mL) and L20B (33.02 ± 2.84 µg/ml).	Bouyahya et al. (2019)
	Infusion extract	CaCo2 and AGS cells.	Inactive	Yemmen et al. (2017)
Antimicrobial activity	Ethanol extract	*Pneumoniae klebsiella*	highest inhibition potential (MIC values of 8 µg/mL).	Carrol et al. (2020)
	Aqueous MeOH extract	*Pneumoniae. gingivalis*	High antimicrobial activity	Mandrone et al. (2019)
	Methanolic extracts	Pork sausage formulation	Reduction of microbial spoilage of fresh traditional pork sausages in the initial stage of storage.	Botsaris et al. (2015)
	Extract and oil	*Staphylococus aureus* and *Aspergillus niger*	Largest spectrum (inhibition zone of 9.33 mm).	Mezni et al. (2015)
Antimutagenic activity	Gallic acid, digallic acid, and 1,2,3,4,6-pentagalloylglucose, polyphenols	*In vitro* assays	Molecules isolated from fruits of *P. lentiscus* induced an inhibitory activity against mutagenicity and genotoxicity	Bhouri et al. (2010) ; Abdelwahed et al. (2007)
Antidiabetic activity	Extract	Streptozotocin-induced diabetic rats	Promising antidiabetic activity, similar to the reference drug glibenclamide (0.91 g/L), a result confirmed by in vitro inhibition of a-amylase.	(Mehenni et al. (2016).

Hepato-protective activity	Extract	Paracetamol [165 mg/kg body weight (b.w.)] toxicity.	Significant protection against paracetamol-induced hepatic necrosis.	Mehenni et al. (2016)
Anti inflammatory Activity	Extract	1β by macrophages exposed to adenosin triphosphate (ATP) or H_2O_2.	Reducetion of the production of IL-1β from ATP- or H_2O_2-activated cells.	Remila et al. (2015)
	Oil	Carrageenan-induced paw edema rat model.	Significant antiinflammatory activity (edema inhibition were 70% and 51.5% ($p < 0.01$), after five hours, significant decreases in the MDA, CAT, SOD, and GPX levels.	Benkhedir et al. (2016)

Conclusion

Plants represent an important source of natural active compounds, such as essential oil, phenols and flavonoids, terpenes and terpenoids that have various therapeutic effects and biological properties. They play a special role from traditional medicine to the discovery of new formulations based on bioactive molecules isolated. In this review, we summarized some existing knowledge about traditional and ethnopharmacological uses of *P. Lentiscus*, phytochemistry and some of its biological activities of its fruits part, mainly focusing on its antioxidant properties, antimicrobial, anticancer, anti-inflammatory, anti diabetic, antimutagenic and hepatoprotective capacities.

P. lentiscus is an important resourceful plant because of its effective pharmacological properties. Studies reported on this specie showed the significance of *P. lentiscus* as a medicinal plant. All data found and summarized in this work indicate that relatively extensive research has been carried out on chemical compounds, pharmacological effects and biological activities of *P. lentiscus* fruits.

Author Contribution Statement

All authors wrote, corrected and contributed to the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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