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Chemical composition, nutritional and health related properties of the medlar (*Mespilus germanica* L.): from medieval glory to underutilized fruit

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Abstract The common medlar (*Mespilus germanica* L.) is one of two species within the Mespilus genus (Maloideae subfamily). Its use can be traced back almost 30 centuries, from ancient Assyrians and Babylonians to Greeks and Romans and through modern times. During the Middle Ages it was a popular fruit tree and a highly appreciated ornamental tree in gardens across Europe. However, in modern times, the medlar is often considered an underestimated and underutilized fruit from the Rosaceae family. Nevertheless, it is slowly regaining its 'medieval glory' and commercial importance as a foodstuff for human consumption. The medlar plant has a wide array of traditional uses in both gastronomy and medicine. Ripe medlar fruits can be consumed fresh or processed into different products such as juice, concentrate, jam, cheese, leather, and honey. Meanwhile, unripe fruits can be used to prepare pickles or beverages such as cider. The nutritional potential of medlar fruits is attributed to sugars, organic acids, fatty acids, carotenoids, amino acids and proteins, vitamins, and essential elements. Scarce literature describes the richness of medlar fruit in bioactive phenolic compounds such as flavonoids and phenolic acids, which contribute to its antioxidant and antidiabetic properties. Additionally, a few studies describe other biological properties of the medlar plant including antimicrobial, cytotoxic and neurodegenerative effects of medlar fruits and leaves, while reports on the clinical studies are lacking. This review paper summarizes the chemical and nutritional properties of medlar fruit, traditional medicinal uses and biological activity of the medlar plant, relying on the most relevant and up to date scientific literature in the field.

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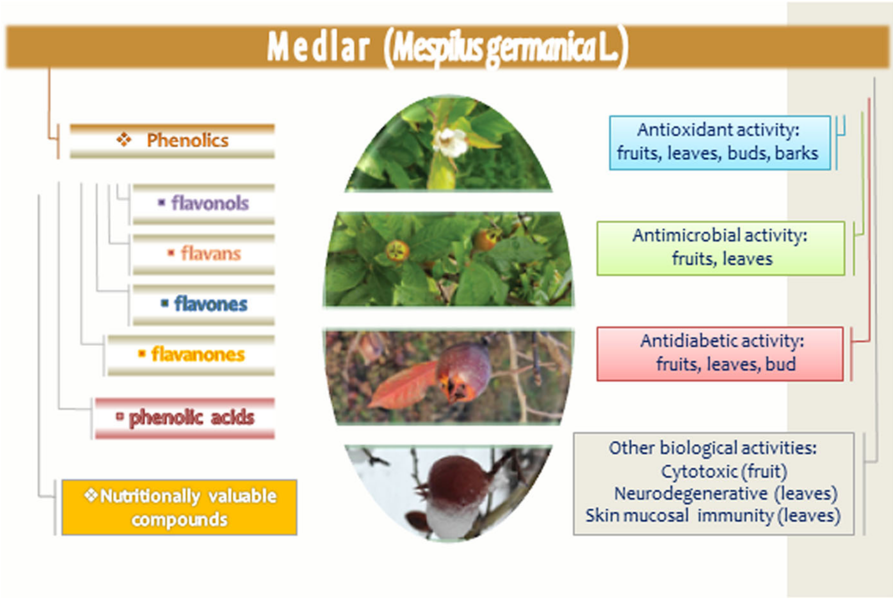
Graphical abstract



Keywords *Mespilus germanica* L. · Neglected fruit · Sugars · Flavonoids · Phenolic acids · Biological properties

Introduction

Mespilus germanica L.

The medlar (*Mespilus germanica* L., *Crataegus germanica* (L.) Kuntze) is an often overlooked fruit in the Rosaceae family, which is composed of over 3000 species and primarily found in the non-tropical region of the Earth's northern hemisphere (Kojić 1984; Kurtto, 2023; PFAF Plant Database). For centuries the medlar was a common fruit tree in central European gardens (Baird and Thieret 1989), and was once the most important fruit crop, until the seventeenth century, when it was surpassed by other, more productive crops. Consequently, medlar cultivation in central Europe has become increasingly rare and is mostly limited to botanical gardens and small farms (Baird and Thieret 1989; Grygorieva et al. 2018). However, there is evidence that medlar fruit is regaining its 'Medieval glory' and commercial importance as a food source for human consumption (Barbieri et al. 2010; Bibalani and Mosazadeh-Sayadmahaleh 2012; Salehi 2020; Joshi and Attri 2017; Yue et al. 2021). Moreover, the medlar plant has been the subject of research for its various biological activities. Most studies report antioxidant activity in different in vitro assays (Akbulut et al. 2016; Campanella et al. 2003; Cevahir and Bostan 2021; Ercisli et al. 2012; Gulcin et al. 2011; Gruz et al. 2011; Isbilir et al. 2019; Katanić Stanković et al. 2022; Nabavi et al. 2011; Ozturk et al. 2022; Rop et al. 2011; Safari and Ahmady-Asbchin 2019; Secilmiş Canbay et al. 2015; Selcuk and Erkan 2015a, b; Tessa et al. 2021), and antimicrobial activity (Ahmady-Asbchin et al. 2013; Bouabdelli et al. 2012; Davoodi et al. 2017; Denizkara et al. 2021; Niu et al. 2013; Tabatabaei-Yazdi et al. 2015) of different parts of the plant. On the other hand, very limited research has been done on the antidiabetic activity of the plant (Isbilir et al. 2019; Katanić Stanković et al. 2022; Żołnierczyk et al. 2021), while preclinical studies are scarce (Aşkar et al. 2022; Kouhestani et al. 2018; Darbandi et al. 2018; Davoudzadeh et al. 2018; Hoseinifar et al. 2017; Katanić Stanković et al. 2022; Shafiee et al. 2018).

The Mespilus genus, belonging to the Maloideae subfamily, includes two widespread species: *M.*

Fig. 1 Morphological features of *M. gemanica* L.: tree **a**, flower **b**, unripe fruit **c** and ripe fruit **d** (Photos by N. Mićanović)

germanica L. (common Medlar) and *M. canescens* J.B. Phipps (Stern's Medlar). The former, which originates from Southeast Asia is the most prevalent species and has been known for centuries. The latter, which comes from North America, was only discovered in 1990. Despite its Latin name, the medlar is mostly found in the Caspian Sea region in the north, in Iran and along the Black Sea coast of modern Türkiye (Voaides et al. 2021). The name germanica (which originates from Line) might not be the most appropriate as the wild medlar is not exclusively found in Germany, and there are only a few cultivated varieties of medlar in the country (Stančević 1986).

Mespilus germanica is a deciduous tree which grows up to 3 m (in the wild) and up to 6 m (cultivated). It is in flower from May to June, and the seeds ripen in November. The species is hermaphrodite (it has both male and female reproductive organs) and is pollinated by bees. The plant is self-fertile. The fruit which appears after flowering is round or pear-shaped; yellow-green to dark brown in color, and it has five large seeds and a cup at the top**,** Fig. 1. It is a typical climacteric fruit. Medlar fruits are harvested very late, in October and early November. Under storage conditions the fruits are placed in a dry cool place until they are over-ripe. During that period the fruits change color to light brown, while flesh softens until the fruits are ready for consumption (Stančević 1986; Sulusoglu Durul and Unver 2016). The fruits also become soft, sweet, and juicy when rotted or frozen. The fruits are edible throughout the winter because they can be stored in an ordinary warehouse for two to three months, and much longer in refrigerators (Stančević 1986). Several varieties are cultivated, depending on the region, such as 'Autumn Blaze', 'Grand Sultan', 'Large Russian', 'San Noyin' and 'Stoneless' (Southeast Europe), 'Comune', 'D'Olanda' and 'Reale' (Italy), 'Breda Giant' (America, Southeast Europe), 'Dutch' (known as 'Giant' or 'Monstrous') and 'Westerveld' (Netherlands), 'Nottingham' (United Kingdom), 'Royal' (France, America), 'Iranian' (Iran) and Marron, (America) (Bibalani and Mosazadeh-Sayadmahaleh 2012; Voaides et al. 2021; Waźbińska 2007). Wild types are also described in literature (Nikolić 2005; Žukovskij 1962). In 1990s, a seedless cultivar named 'Pomoravka' was found in Serbia. Later, the cultivar became commercial in Montenegro. It is a genotype with small fruits but with high stone/fruit ratio (96.5%) (Nikolić 2005; Šebek et al. 2017).

In native speech, names of this fruit are medlar or common medlar (English), mušmula (Serbian), muşmula (Turkish), Azgil tree (Persian), Deutsche mispel or mispel (German), Néflier (French), mispel (Swedish), etc. (Global Biodiversity Information Facility (GBIF)). Besides being consumed as fresh fruit, in the form of snacks, appetizers, combined with wine, prepared in different ways (baked with butter, in cakes and pastries), fresh fruit is used for the preparation of jam, marmalade, jelly, wine, vinegar, juice, refreshing pizzas, sweets, tarts and compotes (Baird and Thieret 1989; Joshi and Attri 2017).

Origin and distribution

Mespilus germanica is a well-known plant native to southwest Asia and southeastern Europe. It grows wild in the Caucasus and Transcaucasus, the southern Crimea, the north-eastern part of Iran, Asia Minor, the Balkan peninsula and Greece. The greatest diversity of forms has been found in Azerbaijan, with some wild forms also found in Turkmenia (Grygorieva et al. 2018; Voaides et al. 2021; Žukovskij 1962). It has been introduced to several countries, including Belgium, France, Great Britain and Northern Ireland, Denmark, the Czech Republic, Portugal, Slovenia, Greece, Ecuador, Romania, Switzerland, and Albania. Besides being established in several European countries, evidence shows that it has been grown in North America (mostly in home orchards or as an ornamental tree), Africa (Egypt, Algeria, Northern Africa and South Africa), Micronesia, South America (Argentina), Australia and New Zealand, Fig. 2 (Baird and Thieret 1989; Global Biodiversity Information Facility (GBIF)).

The medlar has been known for nearly three millennia, from ancient Assyrians and Babylonians to Greeks and Romans up to modern times. It is believed that this fruit (non-native to Europe), which is not native to Europe, was introduced during the Roman era. Although archaeobotanical remains of medlar are generally scarce, some evidence of *Mespilus* has been found in archeological sites in Germany, France, Great Britain, and Switzerland indicating its widespread distribution during the Roman Empire. In later centuries, the fruit became more widely recognized (Pollman and Jacomet 2012), as evidenced by written material and paintings depicting the medlar as a central motif, as shown in Fig. 3. These sources suggest that the medlar was particularly popular in Europe during the Middle Ages (Baird and Thieret 1989; Bol 1977; BBC Future 2021).

The medlar was also mentioned in Shakespeare's plays as well as in agricultural books written by Pietro de' Crescenzi. It was a popular and highly appreciated ornamental tree in gardens throughout the United Kingdom, and a cultivated fruit tree in England's orchards during the seventeenth and eighteenth centuries. Despite its former popularity, the medlar is now often considered a neglected or forgotten fruit throughout Europe (Baird and Thieret 1989).

Lately, neglected and underutilized plant species in horticultural and ornamental systems have been receiving more attention from researchers. This is because these plants offer an alternative in addressing the issues related to food and sustainability of

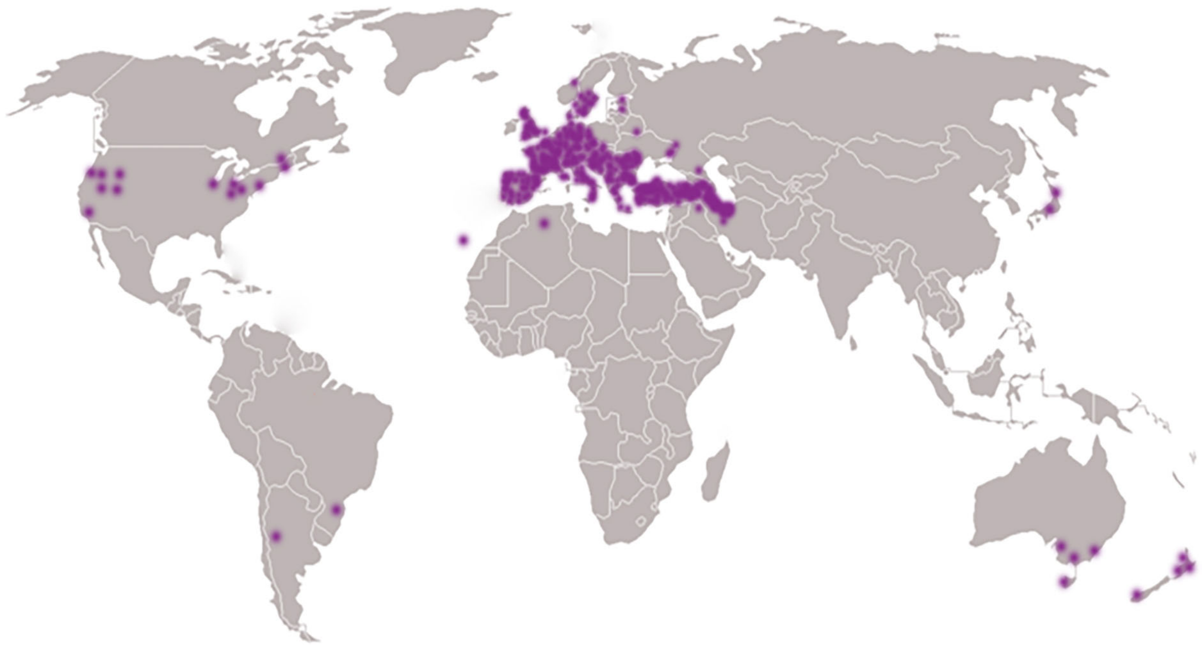


Fig. 2 Distribution of the medlar (*M. germanica* L.) (Adapted according to Global Biodiversity Information Facility (GBIF))

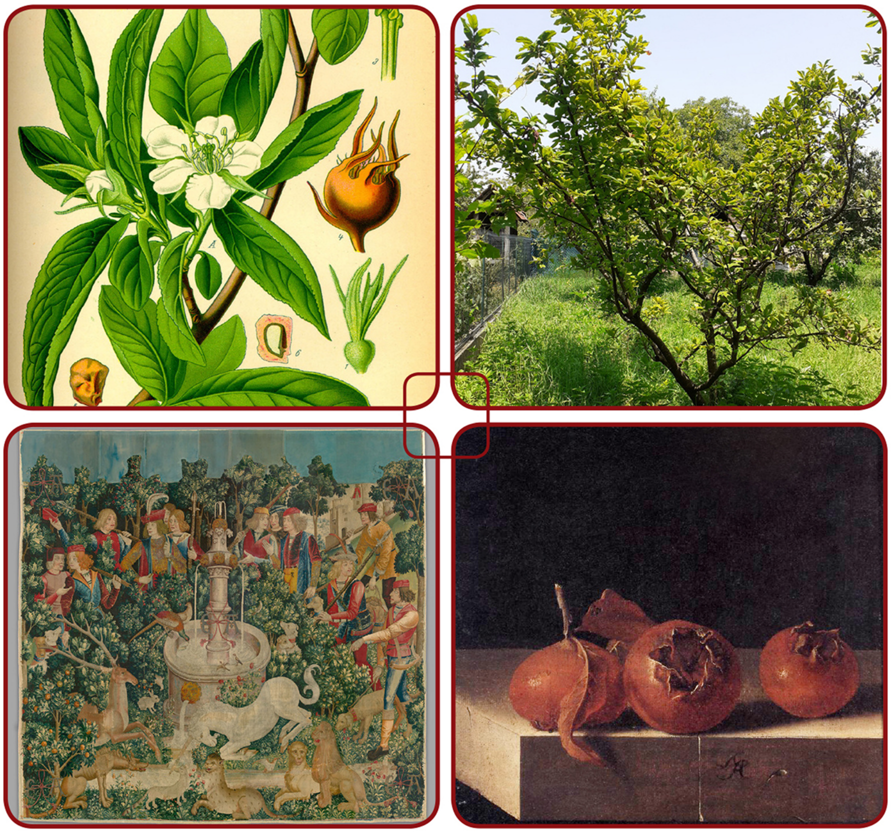


Fig. 3 Collage picture depicting popularity of the medlar; drawing of morphological characteristics of the fruit (upper left), as an ornamental tree (upper right; photo by J. Popović-Djordjević), in the famous tapestry "The unicorn at the fountain" (around 1500) (bottom left) and in the painting "Still life with three medlars" (1705) by Dutch painter Adriaen Coorte (bottom right) (adapted according to https://commons.wikimedia.org/wiki/File:Illustration_Mespilus_germanica0.jpg; https://www.metmuseum.org/art/collection/search/467638 and https://commons.wikimedia.org/wiki/File:Adriaen_Coorte_-_Three_Medlars_with_a_Butterfly_-_WGA05210.jpg)

agricultural production. With the world's population on the rise, climate change and the depletion of natural resources, these plant species can play a vital role in increasing biodiversity, enhancing the resistance of agro-ecosystems to environmental stresses, and serving as a foundation for functional foods. Moreover, they can be used for decorative purposes and landscape design (Mauro et al. 2022). Among these species, *M. germanica* stands out as a promising fruit species offering diverse nutritional and health benefits.

Use of the medlar plant and health effects

Medlar fruits have various traditional uses both in the field of gastronomy and in medicine. Regarding gastronomy, ripe medlar fruits can be consumed fresh (Rop et al. 2011; Ozturk et al. 2019) or they may be processed into different products including juice, concentrate (Salehi 2020), jam, cheese (Bibalani and Mosazadeh-Sayadmahaleh 2012), leather (Suna 2019) and honey (Yue et al. 2021). Moreover, unripe fruits can be used to prepare pickles (Bibalani and Mosazadeh-Sayadmahaleh 2012) or beverages such as cider (Barbieri et al. 2010). On the other hand, fruit seeds are not suitable for consumption as they are reported to be poisonous (Bibalani and Mosazadeh-Sayadmahaleh 2012). Table 1 presents the traditional medicinal uses of the medlar plant. Various parts of the medlar are utilized for medicinal purposes in Türkiye, Iran, Algeria, and Serbia. Freshly consumed medlar fruit is suggested to be effective against diarrhea (Kültür 2007; Jarić et al. 2015; Paksoy et al. 2016), inflammation (Miser-Salihoglu et al. 2010) and

Table 1 Traditional medicinal use of the medlar plant (*M. germanica* L.)

Location	Local name	Part(s) used	Preparation	Disease(s) treated/Benefits	References
Kırklareli, Türkiye	Muşmula,	Fruits	Fresh	Diarrhea	Kültür (2007)
	Yabani muşmula	Leaves	Decoction	Cough, cold, flu	
Düzce, Türkiye	Töngel, Döngel, Beşbıyık, Muşmula	Fruits	Ns	Inflammations	Miser-Salihoglu et al. (2010)
		Leaves		Diarrhea, Cough, Rheumatism, Diabetes, Hemorrhoids	
Gilan, Roudsar, Iran	Kounos	Fruits	Sodden	Large intestine infection, Diarrhea, Internal hemorrhage, Cholera, Stomach bloating, Cold and dryness, Fattening, Menstrual irregularities/ Hematopoietic, Nerve strengthening, Diuretic	Bibalani and Mosazadeh-Sayadmahaleh (2012)
		Leaves	Sodden	Large intestine infection, Diarrhea, Internal hemorrhage, Cutaneous leishmaniasis, Cold and dryness, Oral abscess/Hematopoietic, Skin strengthening, Throat treatment	
		Bark	Dry powder	Large intestine infection, Diarrhea, Internal hemorrhage, Fever/Hematopoietic, Diuretic	
		Wood	Dry powder	Fever	
Western Algeria	Zaarour	Leaves	ns	Hypoglycemia/Anti-lithiasis	Bouabdelli et al. (2012)
Suva planina, Serbia	Mušmula	Fruits	Fresh	Diarrhea/Improvement of eyesight, liver and kidney performance	Jarić et al. (2015)
Istanbul, Türkiye	Muşmula	Fruits	Fresh	Constipation/Treatment of kidney and bladder of stones	Koçyiğit et al. (2015)
		Pulp	Syrup	Enteritis	
		Leaves	Decoction	Diabetes	
		Bark	Decoction	Abdominal pain/Anthelmintic	
Ulukışla, Niğde, Türkiye	Muşmula	Fruits	Fresh	Diarrhea	Paksoy et al. (2016)
Mazandaran, Iran	Azgil, Kondes	Fruits, leaves	Decoction	Stomachache, Dysentery, Vomiting/ Hypoglycemic agent	Ahvazi and Akbarzadeh (2017)
Adana, Türkiye	Muşmula	Fruits, leaves	Infusion	Asthma, Hepatitis	Güneş et al. (2017)
Türkiye	Ns	Fruits, leaves	Infusion	Influenza	Sargin (2021)

Ns: Not specified

constipation (Koçyiğit et al. 2015). Consumption of fresh medlar fruit has also been linked to improvement in eyesight, liver and kidney function, and treatment of kidney and bladder stones (Jarić et al. 2015; Koçyiğit et al. 2015). Apart from fresh consumption, medlar fruit infusion is also used for medicinal purposes. It has been reported to be effective against large intestinal infection, diarrhea, internal hemorrhage, cholera, stomach bloating, cold and dryness, fattening, and menstrual irregularities. Medlar fruit infusion also has hematopoietic, nerve strengthening and diuretic effects (Bibalani and Mosazadeh-Sayadmahaleh 2012). Additionally, syrup prepared from medlar fruit pulp shows potential for use against enteritis (Koçyiğit et al. 2015). While most studies do not provide specific information regarding the suggested dose for consumption, Kültür (2007) recommends eating one to two pieces of fruit twice a day for five days in order to achieve the desired effect.

In addition to the fruit itself, decoctions prepared from medlar leaves are utilized against cough, cold, flu, diarrhea, rheumatism, diabetes, hemorrhoids, large intestinal infections, internal hemorrhage, cutaneous leishmaniasis, oral abscess and hypoglycemia (Kültür 2007; Miser-Salihoglu et al. 2010; Bibalani and Mosazadeh-Sayadmahaleh 2012; Bouabdelli et al. 2012; Koçyiğit et al. 2015). Medlar leaves are also consumed for their hematopoietic, skin strengthening, throat treatment and anti-lithiasis effects (Bibalani and Mosazadeh-Sayadmahaleh 2012; Bouabdelli et al. 2012). Furthermore, infusions prepared with leaves and fruits are used for the treatment of stomachache, dysentery, vomiting, hypoglycemia, asthma, hepatitis, and influenza (Ahvazi and Akbarzadeh 2017; Güneş et al. 2017; Sargin 2021). As is the case with fruits, only a few studies reported a consumption dosage for leaf decoctions. Kültür (2007) advised to drink one teacup twice a day 7–10 days, whereas Güneş et al. (2017) suggested the consumption of one cup thrice a day in order to see the beneficial effects.

The bark and wood of the medlar plant are traditionally used both as a powder and decoction. Medlar bark and wood powder are reported to be effective against large intestinal infection, diarrhea, internal hemorrhage and fever, and also have hematopoietic and diuretic effects (Bibalani and Mosazadeh-Sayadmahaleh 2012). Similarly, decoction prepared with medlar bark is said to have anthelmintic effects and can relieve abdominal pain (Koçyiğit et al. 2015). Overall, although studies on the traditional medicinal uses of the medlar plant are limited, they suggest that different parts of this plant may have various medical applications.

Chemical composition of medlar fruit

In addition to the well-known and examined fruit species there are some neglected and/or unexamined species which are good sources of phytochemicals such as the medlar (*M. germanica* L.). Due to its limited growing area, the medlar remains unrecognized in the wider scientific community, but it is well known among people in southeastern Europe, Türkiye, Iran and Iraq, the part of the world where the plant originates from. The complex chemical composition makes the medlar a nutritionally important fruit.

However, data about the chemical composition and biological properties of wild-growing and/or cultivated medlar fruits are limited. Literature related to the nutritional evaluation of medlar fruits mainly provides data on dry matter, total sugars (reducing and complex), vitamin C, crude proteins (Ercisli et al. 2012; Šebek et al. 2019; Waźbińska 2007), fatty acids (Ayaz et al. 2002), carotenoids (Olives Barba et al. 2006), as well as macro (K, Ca, Mg, Na, P) and microelements (Fe, Mn, Zn, Cu, B) (Glew et al. 2007; Azizi 2011; Pető et al. 2016). Differences observed in the content of nutrients between medlar fruits are attributed to cultivar differences, environmental conditions, maturity stage, growth stage, and soil fertilization (Ercisli et al. 2012; Azizi 2011; Pető et al. 2016; Waźbińska 2007). Recently, bioactive compounds in medlar fruits such as polyphenols (phenolic acids, flavonoids) have become a subject of increasing interest among researchers (Akbulut et al. 2016; Gruz et al. 2011; Gulcin et al. 2011; Katanić Stanković et al. 2022; Ozturk et al. 2019; Rop et al. 2011; Żołnierczyk et al. 2021). Apart from being a good source of phenolics, the nutritional composition of the fruits encompasses sugars (glucose, sucrose, fructose, pectines, etc.), organic acids (malic, tartaric, oxalic, citric, etc.), vitamins (C, E) (Al-Amoudi et al. 2019; Akbulut et al. 2016; Cevahir and Bostan 2021; Cosmolescu et al. 2020; Ercezli et al. 2012; Glew et al. 2003a; Tessa et al. 2021), fatty acids (Glew et al. 2003a; Veličković et al. 2013; Voronkov et al. 2020), essential elements (Glew et al. 2007; Ercezli et al. 2012; Pető et al. 2016; Żołnierczyk et al. 2021), amino acids, and proteins (Haciseferogullari et al. 2005; Glew et al. 2003b), and volatile compounds (Tessa et al. 2021; Veličković et al. 2013). Overview of the studies related to the chemical composition of the medlar fruit and relevant alanalytical methods are presented in Table 2.

Some general and proximate parameters of several medlar cultivars collected in Montenegro (Bijelo Polje) important for preliminary fruit quality determination were evaluated by Šebek et al. (2019). Authors found that dry matter in the medlar fruit ranged from 26.2 to 28.8%, while total soluble solids (SS) varied from 20.45 to 22.25%. In addition, all fruits possessed

Table 2 Phytochemical profile of medlar fruits and seeds and analytical methods

Class of compounds	Analytical technique*	Obtained results	References
Phenolics	UHPLC/(−)HESI–MS/MS	12 phenolic compounds in fresh fruit ethanolic extract (expressed in mg/kg of dry weight): aesculetin (4.65), rutin (2.92), quercetin-3-*O*-glucoside (11.71), kaempferol-3-*O*-glucoside (3.12), quercetin-3-O-rhamnoside (14.04), quercetin (2.00), pinocembrin (0.44), *p*-coumaric acid (3.53), protocatechuic acid (12.91), syringic acid (10.24), chlorogenic acid (78.81) and caffeic acid (8.55)	Katanić Stanković et al. (2022)
	HPLC–DAD	Water extract of fresh fruit (expressed in mg/g dry weight): 5 phenolic acids (caffeic, chlorogenic, *p*-coumaric, cinammic, ferulic), 2 flavonoid aglycones (quercetin, kaempferol) and 1 glycosides (rutin) were quantified in range from 0.05 (chlorogenic acid) to 38.75 (rutin)	Sadeghinejad et al. (2022)
	HPLC–DAD	Homogenized fresh fruits (expressed in mg/100 g of fresh weight); Catechins: catechin (1.05), epicatechin (1.11), Benzoic acids: ellagic acid (1.2), gallic acid (2.32), Flavonols: quercetrin (2.14), quercitrin (1.15), rutin (12.51) Cinnamic acids: caffeic acid (6.21), chlorogenic acid (16.75), coumaric acid (5.94), ferulic acid (2.77)	Tessa et al. (2021)
	UPLC/DAD	80% ethanolic extract of lyophilized fruit acidified with hydrochloric acid (expressed in mg/g of dry weight): gallic acid (8.8), *p*-aminobenzoic acid (1.2), protocatechuic acid (0.6), catechin (0.9), (-)epicatechin (7.9), chlorogenic acid (3.0), neochlorogenic acid (5.3), procyanidin B (3.5), caffeic acid (0.4), ferulic acid (1.0) sinapic acid (0.1)	Zołnierczyk et al. (2021)
	HPLC_DAD	medlar fruit pulp (expressed in mg/kg of fresh weight): gallic acid (18.6), protocatechuic acid (11.1), catechin (3.1), quercetin (10.9), chlorogenic acid (91.5), caffeic acid (4.5), ferulic acid (11.1)	Ozturk et al. (2019)
	HPLC–DAD	Fresh fruit extract in a mixture of hydrochloric acid, methanol, ACS water (v/v ratio- 2:80:18) (expressed in mg/100 g fresh weight): 9 major phenolic compounds - chlorogenic acid (8.35–11.74), rutin (4.45–6.48), *p*-coumaric acid (4.35–6.14), *p*-aminobenzoic acid (2.30–3.01), quercetin (1.30–1.62), vanillin (0.95–1.24), protocatechuic acid (0.80–1.14), gallic acid (0.75–1.18), caffeic acid (0.86–1.42) 5 minor phenolic compounds - catechin (0.25–0.51), ferulic acid (0.19–0.52), epicatechin (0.29–0.52), resveratrol (0.16–0.41), quercitrin (0.09–0.22)	Akbulut et al. (2016)
	LC–MS/MS	Lyophilized aqueous extract of medlar fruits (expressed in mg/kg of dry weight): caffeic acid (4.9), ferulic acid (2.4), ellagic acid (0.2), quercetin (2.4), pyrogallol (3.6), *p*-coumaric acid (2.4)	Gulcin et al. (2011)
	HPLC–UV-Vis	Fresh fruit extract in a mixture of hydrochloric acid, methanol, ACS water* (v/v ratio—2:80:18) (expressed in mg/100 g of fresh weight): In total, 13 phenolic compounds were identified and quantified - rutin, quercitrin, resveratrol, catechin, epicatechin, vanillin, *p*-coumaric acid, caffeic acid, ferulic acid, gallic acid, protocatechuic acid, *p*-aminobenzoic acid, chlorogenic acid	Rop et al. (2011)

Table 2 continued

Class of compounds	Analytical technique*	Obtained results	References
	HPLC–MS	In total 8 different acids were quantified. Phenolic acid profile depended on the type of extraction applied i.e. on type of isolated phenolic fraction: Fraction of free phenolic acids- Protocatechuic acid and 4-hydroxybenzoic acid (the most abundant), 4-hydroxybenzoic acid, syringic acid, caffeic acid, sinapic acid Ester-bound soluble fraction- caffeic acid (the most predominant), protocatechuic acid, syringic acid, caffeic acid, 4-hydroxybenzoic acid, 3-hydroxybenzoic acid, sinapic acid Ester-bound insoluble fraction: protocatechuic acid (the most abundant), 4-hydroxybenzoic acid, 3-hydroxybenzoic acid, salicylic acid, 4-coumaric acid, caffeic acid	Gruz et al. (2011)
Organic acids	HPLC–DAD	Homogenized fresh fruits (expressed in mg/100 g of fresh weight); citric acid (380.99), malic acid (406.5), oxalic acid (59.35), tartaric acid (116.2)	Tessa et al. (2021
	HPLC-RI	Fresh homogenized fruits (expressed in mg/100 g of fresh weight): malic acid (590.5–1074.5) succinic acid (127.0–419.0) citric acid (2.0–32.0)	Cevair and Bostan (2021)
	HPLC–UV	Fresh homogenized fruit pulp diluted with 2% hydrochloric acid (expressed in mg/100 g of fresh weight): oxalic acid (54.73), tartaric acid (111.6), malic acid (415.1), citric acid (16.4), fumaric acid (0.8)	Cosmolescu et al. (2020)
	GLC	Lyophilized fresh fruit pulp (expressed in g/100 g of dry weight): malic (1.7–3.4), citric (0.01–0.1), quinic (1.3–1.9), succinic (0.02–0.03)	Cristofori et al. (2019)
	HPLC–DAD	Medlar fruit pulp (expressed in mg/kg of fresh weight): oxalic acid (1118.1), citric acid (5537.4), malic acid (7166.2), fumaric acid (20.1)	Ozturk et al. (2019)
	HPLC–UV-Vis	Fresh homogenized fruits (expressed in mg/100 g fresh weight): malic acid (1733/0 day–1150/60 day), succinic acid (570/0 day–428.3/60 day), quinic acid (534.6/0 day–341.0/ 60 day), oxalic acid (35.3/0 day–25.1/60 day), citric acid (21.7/0 day–3.4/60 day)	Selcuk and Erkan (2015a)
	HPLC/UV	Ethanolic extract of fresh fruit pulp (expressed in mg/100 g of fresh weight): First week after harvesting - citric acid (420.2), malic acid (434.0)	Glew et al. (2003a)
	HPLC–UV	Ethanolic extract of seedless fresh fruit pulp (expressed in mg/100 g of fresh weight): malic acid (126.0–428.0) citric acid (528.0–404.0) ascorbic acid decreased ↓(41.7–8.4) malic acid increased ↑, citric acid ↓ during maturation	Glew et al. (2003b)
Sugars	HPLC-RI	Fresh homogenized fruits (expressed in mg/100 g fresh weight): fructose (3255–4726), glucose (2108–3017), sucrose (127–399)	Cevahir and Bostan 2021
	GLC	Lyophilized fresh fruit pulp (expressed in g/100 g of dry weight): fructose (29.6–32.6), glucose (17.4–21.4), sucrose (0.02–0.03), sorbitol (4.5–6.3)	Cristofori et al. (2019)

Table 2 continued

Class of compounds	Analytical technique*	Obtained results	References
	HPLC-RI	Fresh homogenized fruits (expressed in mg/100 g fresh weight): fructose (7366—0 day),(7647—60 day); glucose (5739—0 day), (5494—60 day)	Selcuk and Erkan 2015a
	HPLC/UV	Ethanolic extract of fresh fruit pulp (expressed in mg/100 g of fresh weight): Results are referring to the first week after harvesting - sucrose (228.4), fructose (2153.1), glucose (738.4)	Glew et al. (2003a)
	HPLC–UV	Ethanolic extract of fresh fruit pulp (expressed in mg/100 g of fresh weight): sucrose (15.0/unripe → 918.0/131 day of maturation → 219.0/161 day (end of maturation)) fructose (197.0/ unripe → 1200.0/end of maturation) glucose (298.0/ unripe → 788.0/69 day of maturation → 686.0/end of maturation) during maturation: sucrose↓, fructose↑, glucose fluctuated	Glew et al. (2003b)
Fatty acids (FAs)	GC–MS	Fresh fruit pulp (expressed in percentage): 14 fatty acids (FAs) were quantified (5 unsaturated FAs and 9 saturated FAs). The shares calculated on total FAs were as follow: linolelaidic acid (24.01%), oleic acid (11.45%), palmitic acid (6.97%), arachidic acid (2.99%), lingoceric acid (2.47%), behenic acid (2.45%), stearic acid (1.78%), palmitoleic acid (0.49%), myristic acid (0.38%), lauric acid (0.37%), cerotic acid (0.26%), linoleic acid (0.22%), margaric acid (0.21%) and phthalic acid (0.13%)	Azizi (2011)
	GC-FID	Oil extracted from fresh fruits with chloroform: methanol (v/v—2:1) with the addition of 0.9% sodium chloride (expressed in µg/g of dry weight) first week after harvesting: C10:0 (6.7), C12:0 (6.8), C13:0 (7.8), C14:0 (9.8), C14:1(9.3), C15:0(3.9), C16:0(420.0), C16:1(8.4), C18:0(68.5), C18:1n-9(249.7), C18:1n-7 (24.5), C18:1n-5(3.6), C18:2n-6 (1340.0), C18:3n-3 (355.6), C20:0 (39.0), C20:1n-9 (4.1), C20:1n-7(9.4), C22:0 (40.1), C22:1n-9 (3.3), C24:0 (24.1)	Glew et al. (2003a)
Amino acids	HPLC	Ethanolic extract of fresh fruit pulp (expressed in mg/g dry weight): the most abundant amino acids in ripe fruit (after 161 day of maturation) were: aspartate (1.13) and glutamate (1.22) During maturation process content of most of 18 analyzed amino acids decreased	Glew et al. (2003b)
Volatile compounds		Homogenised fresh fruits (expressed in mg/100 g of fresh weight); Monoterpenes: phellandrene (377.82), γ-terpinene (922.77), terpinolene (79.67)	Tessa et al. (2021)
	GC–MS	Crude oil extracted from fresh fruits in CH_2Cl_2 (unripe and ripe): In total 32 compounds were quantified; 3 alcohols, 10 aldehydes, 5 organic acids, 4 esters, 10 terpenes The most predominant were C-6 aldehydes and alcohols Hexanol (42.57%) was the predominant volatile in ripe fruit while hexanal (32.81%) and 2-hexenal (43.47%) prevailed in the unripe fruit	Veličković et al. (2013)
	GC–MS	Extract of dried medlar seeds with liquid carbon dioxide under 200 atm pressure and 45 °C temperature: 3 volatile compounds were quantified: benzaldehyde (98.5%), pentadecane (1.08%) and tetradecane (0.43%)	Pourmortazavi et al. 2005

Table 2 continued

Class of compounds	Analytical technique*	Obtained results	References
Ascorbic acid	HPLC-RI	Fresh homogenized fruits: 21.5—44.2 mg/100 g of fresh weight	Cevair and Bostan (2021)
	HPLC–DAD	Homogenized fresh fruits (expressed in mg/100 g of fresh weight): ascorbic acid (6.04) dehydroascorbic acid (13.43)	Tessa et al. (2021)
	HPLC–UV	Fresh homogenized fruit pulp diluted with 2% hydrochloric acid: 0.7 mg/100 g of fresh weight	Cosmolescu et al. (2020)
	HPLC–DAD	Medlar fruit pulp: 227.1 mg/kg of fresh weight	Ozturk et al. (2019)
	HPLC-DA	Fresh homogenized fruits: 12.1 mg/100 g fresh weight /0 day and 0.94 mg/100 g fresh weight /60 days Decreased after 60 days ↓	Selcuk and Erkan (2015a)
	LC–MS/MS	Lyophilized aqueous extract of medlar fruits: 186.4 mg/kg of dry weight	Gulcin et al. (2011)
	HPLC-ED	Fresh fruit extract in a mixture of hydrochloric acid, methanol, ACS water (v/v ratio–2:80:18): 59.0 mg/100 g of fresh weight /134 day-17.0 mg/100 g of fresh weight / 174 day after full bloom	Rop et al. (2011)
	HPLC/UV	Ethanolic extract of fresh fruit pulp first week after harvesting: 9.0 mg/100 g of fresh weight	Glew et al. (2003a)
	HPLC–UV	Ethanolic extract of seedless fresh fruit pulp: 41.7–8.4 mg/100 g of fresh weight decreased during maturation	Glew et al. (2003b)
α-tocopherol	LC–MS/MS	Lyophilized aqueous extract of medlar fruits: 13.4 mg/kg of dry weight	Gulcin et al (2011)
β-carotene	HPLC–UV-Vis	Fresh homogenized fruits: 0.9–1.0 mg/ 100 g of fresh weight	Olives Barba et al. (2006)

**UHPLC/(−)HESI–MS/MS–Ultra-High performance liquid chromatography with heated electrospray ionization coupled to tandem mass spectrometry; LC–MS/MS–Liquid chromatography/ mass spectrometry; HPLC–DAD–High-Performance Liquid Chromatography with Diode-Array Detection; UPLC–Ultra performance liquid chromatography; GC-FID–Gas chromatography with Flame Ionization Detector; GLC–Gas liquid chromatography; GC–MS–Gas chromatography with mass detector; HPLC–MS–High-performance liquid chromatography with mass detection; HPLC-ED–High-performance liquid chromatography with electrochemical detection; HPLC–UV-ViS–High-pressure liquid chromatography with UV/Visible detector; HPLC-RI–High-pressure liquid chromatography with refraction index detector;

**ACS water—chemical meeting the specifications of the American Chemical Society, Sigma-Aldrich, USA

moderate acidity (pH 3.40–3.86) while total acidity was in the range from 1.9 to 2.28%. Similar results for SS were obtained for different medlar genotypes collected in Türkiye (Coruh valley): 16.4–21.4%, whereas crude protein content was in the range from 3.3 to 4.1%, while ascorbic acid (vitamin C) content varied from 11.3 to 15.0 mg/100 g of fresh weight, depending on the variety (Ercisli et al. 2012). Importance of the analyzed genotype, but also possibly geographical location, for SS and crude protein content was confirmed in another study from Türkiye (Antalia region) where authors determined 23.97% for

SS and 1.06% for crude protein (Kalyoncu et al. 2013). The given results were higher (SS) i.e. lower compared to the results obtained by Ercisli et al. (2012). They also found that the medlar fruits were acidic (pH 4.29) similar to the study from Montenegro. Acidity of the medlar fruit decreased during storage for 60 days while pH was increased from 3.2 to 3.5 (Selcuk and Erkan 2015a). To prevent the loss of medlar fruit quality, authors recently suggested application of modified packaging atmosphere (MAP) as well as the application of methyl jasmonate, while a combined application of MAP and methyl jasmonate prevents loss of oxalic, ascorbic and citric acids. It was observed that MAP significantly reduced loss in total phenolics, flavonoids as well as antioxidant activity (Ozturk et al. 2019). Medlar fruit powder could be used as a functional additive, in order to improve selected physico-chemical and sensory properties of sponge cookies enriched with this powder. Addition of powder improved hardness of cookies as well as shelf life. In addition, application of medlar fruit powder significantly increased crumb redness value. It was also observed that the addition of medlar fruit powder significantly increased total phenolic content in the cake as well as its antioxidant properties measured via ability to quench DPPH free radicals (Uçar and Hayta 2018).

Main classes of compounds in medlar fruits

Nutritionally significant compounds

Organic acids Various organic acids (OAs) are found in fleshy parts of all fruits and their content varies between fruit species as well as cultivars. The taste of fruits and their usage in different fruit products are mainly attributed to OAs. Some fruits are rich malic, citric, isocitric, galacturonic, quinic, oxalic, and tartaric acids, whereas phenolic acids and ascorbic acid are omnipresent in fruits (Walker and Famiani 2018). According to literature, main OAs detected in medlar fruits are: oxalic, succinic, fumaric, malic, tartaric, citric and quinic, Table 2, Fig. S1 (in Supplementary Information—SI) (Cosmolescu et al. 2020; Glew et al. 2003a, b; Ozturk et al. 2019; Selcuk and Erkan 2015a; Tessa et al. 2021; Voaides et al. 2021). Besides environmental factors and cultivation practices, the content of individual acids is attributed to the stage of fruit ripeness as well as storage time after the harvest period. Literature data indicate that the content of OAs declines in over-ripe fruits and during prolonged storage period (Glew 2003a; Famiani et al. 2015; Selcuk and Erkan 2015a). Reduction of OA content during storage may be prevented using specific storage systems such as palliflex controlled atmosphere storage containing 2% O_2 + 5% CO_2. Prevention of OA loss contributes to the overall fruit taste and its quality (Selcuk and Erkan 2015a). Both the nature and the concentration of organic acids greatly affect the organoleptic quality such as taste, sight, and smell (Batista-Silva et al. 2018).

Sugars Medlar fruit is rich in carbohydrates. Some authors have reported 23–73% of carbohydrates in fresh fruits (Cevahir and Bostan 2021; Sabry and Rizek 1982; Vargas et al. 2009). The principal sugars detected in medlar fruits are fructose, glucose, and sucrose, Table 2 (Aydin and Kadiouglu 2001; Glew et al. 2003a; Selcuk and Erkan 2015a) whereas Baird and Thieret (1989) reported xylose, Fig. S2 (SI). Aydin and Kadiouglu (2001) reported data on the changes in soluble sugar content (pentose and hexose) during the development and ripening of medlar fruit, but no specific sugars were studied except glucose. Recently, sorbitol (D-glucitol) has been reported in four medlar varieties grown in Regione Lazio, Italy, Fig. S2 (SI) (Cristofori et al. 2019). Sorbitol is a sugar alcohol naturally present in fruits and vegetables. It has a sweet taste, a low glycemic index and benefits related to anti-hyperglycemic properties, as it does not elevate plasma glucose. Hence, it is widely used in sugar-free foods and products intended for diabetics (Nontokozo et al. 2021). Structural analysis of pectins isolated from medlar fruit revealed the presence of D-galacturonic acid, L-arabinose, L-rhamnose, D-galactose and D-glucose (Al-Amoudi et al. 2019). Similar to OAs, the content of sugars is affected by a series of factors, including cultivar/genotype, region of cultivation, and the development and ripening periods (Aydin and Kadiouglu 2001; Cristofori et al. 2019; Voaides et al. 2021). The accumulation of sugars characterizes the ripening period of many climacteric species. Changes in the content of fructose and glucose (increase) and sucrose (decrease) has been observed. On the other hand, during that period, the content of OAs decreases (Batista-Silva et al. 2018). In medlar fruit (a typical climacteric fruit) the same trend has been observed (Aydin and Kadiouglu 2001; Glew et al. 2003a). Also, the content of the main sugars gradually changes in the post-harvest period (Glew et al. 2003a).

Volatile compounds Although they are present in very small concentrations, volatile aroma compounds contribute to the specific flavor of a certain fruit. Lipid compounds, as assumed to be precursors of volatile compounds, are mainly associated to aroma during fruit ripening. Structures of major volatile compounds in medlar fruit and seed are presented in Fig. S3 (SI). The only study on volatiles in medlar fruits indicated that the main volatile compounds in unripe (green) and ripe fruits were C6 aldehydes (hexanal, furfural and (*E*)-2-hexenal) and alcohols (hexanol and (*Z*)-3-hexenol). It was noticed that the content of hexanal and (*E*)-2-hexenal declined in ripe fruits (compared to unripe ones), while the content of furfural was substantially higher in ripe fruits. On the other hand, the content of alcohols was increased in ripe fruits (Veličković et al. 2013). Fatty acids and their esters were developed during the ripening period (observed based on their content). Among terpenes, in both unripe and ripe fruits, predominant were *p*-cymene, terpinen-4-ol, γ-terpinene and γ-eudesmol. Phellandrene and α-terpinene were detected only in unripe and ripe fruits, respectively, in considerable amounts, while other terpenes were detected only in trace amounts (Veličković et al. 2013). In the study of Tessa et al. (2021), γ-terpinene and phellandrene were the most dominant volatiles of ripe fruits. In medlar seeds (unlike fruits) only three volatile compounds were detected; benzaldehyde (> 98%), pentadecane and tetradecane, Table 2 (Pourmortazavi et al. 2005).

In addition to volatile terpenes, medlar fruits contain tetreterpenoids such as carotenoids. Among them β-carotene (provitamin A) is the most dominant one (Fig. S5, SI). Carotenoids exibit antioxidant properties and their dietary intake is linked to the reduced risk of some diseases such as cancer, eye degeneration and neuronal damage. In two medlar varieties concentrations of β-carotene were comparable to its content in some tomato varieties, Table 2 (Olives Barba et al. 2006).

Because of the economic interest, organoleptic features are the focus of many research studies aiming to improve fruit quality. Most prominent characteristics that are of special importance for fruit quality are nutritional value and sensorial attributes (e.g. visual feature, hardness and flavor). Additionally, deliciousness which is principally influenced by the balance between organic acid (acidity) and sugar content (sweetness) is suspected to be of major metabolic significance (Batista-Silva et al. 2018). The main modifications noticed during ripening are linked to the alteration of sugars, organic acids, and volatile compounds and they are visually observed as color and textural changes. Such modifications fully contribute to fruit flavor, especially by adjusting the balance between sugar and organic acids (Batista-Silva et al. 2018; Famiani et al. 2015). It is reported in literature that the taste and flavor of some Rosacea family fruits are mainly attributed to monoterpenes (volatiles) and organic acids (Tessa et al. 2021).

Fatty acids According to the absence or presence of double bond fatty acids (FAs) they can be classified as saturated and unsaturated FAs, respectively. In addition, naturally occurring unsaturated fatty acids (UFAs) have *cis* configuration of a double bond, whereas *trans* configuration occurs in products as a result of technology processing. Omega-3 (ω-3) and omega-6 (ω-6) polyunsaturated fatty acids (PUFAs) are essential and have to be taken through food consumption. Due to their significant roles in metabolic processes which result in health benefits, ω-3 and ω-6 FAs have been considered as functional food and nutraceuticals (Dąbrowska et al. 2019; Murathan et al. 2016; Orsavova et al. 2015). Chemical structures of fatty acids detected in medlar fruits are presented in Fig. S4 (SI).

Saturated fatty acids (SFAs) such as hexanoic (caproic—C6:0), dodecanoic (lauric—C12:0), tetradecanoic (myristic-C14:0), pentadecanoic (pentadecylic—C15:0), acids were reported in ripe fruits, with C6:0 and C16:0 as predominant ones, while hexadecanoic acid (palmitic—C16:0) was detected in both unripe and ripe fruits (Veličković et al. 2013). Moreover, other FAs described in literature were octadecanoic (stearic—C18:0), 9-octadecenoic (oleic—C18:1), 9,12-octadecadienoic (linoleic—C18:2), *trans*-9,12-octadecadienoic (linolelaidic—C18:2), eicosanoic (arachidic- C20:0) and docosanoic (behenic—C22:0), tetracosanoic (lignoceric—C24:0) acids (Azizi 2011; Voronkov et al. 2020). Besides major SFAs and UFAs (palmitic, stearic, oleic linoleic and linolenic) Glew et al. (2003) detected less common ones (C10-15, C16:1, C20-24), Table 2. Veličković et al. (2013) reported esters of C16 and C18 FAs, ethyl-hexadecanoate and ethyl-oleate, in ripe medlar fruits from Serbia, confirming biogenetic formation of SFAs and UFAs during the ripening process and their transformation to the corresponding esters.

Vitamins Fruits are well known sources of vitamins: C (ascorbic acid), A, B1 (thiamine), B3 (niacin), B6 (pyridoxine), B9 (folacin or folic acid) and E. Unlike macronutrients (carbohydrates, lipids, and proteins) which are needed to provide energy. Vitamins play an essential role in energy metabolism, as coenzymes. They are involved in energy release and storage. Vitamins A, C and E have pronounced antioxidant properties (Kader 2002). Most studied vitamins in medlar fruits are ascorbic acid (vitamin C), dehydroascorbic acid and α-tocopherol (vitamin E), Table 2, Fig. S5 (SI) (Akbulut et al. 2016; Cevahir and Bostan 2021; Cosmolescu et al. 2020; Glew et al. 2003a; Gulcin et al. 2011; Ercezli et al. 2012; Selcuk and Erkan 2015a).

Biogenic and other elements Major (K, Ca, Mg, P) and trace elements (Fe, Mn, Cu, Zn) are important in human nutrition. Although they are not taken in large quantities, the normal functioning of a living organism depends on these elements, and therefore must be regularly present in the diet (Callahan et al. 2020; Popović-Djordjević et al. 2022). Major elements constitute the bones and the teeth (Ca, P), they act as muscle relaxants (Mg), maintain fluid and electrolyte balance and help the functioning of the nervous system (K). On the other hand, trace elements are an integral part of many enzymes and play a crucial role in many biological processes, supporting normal growth and development in pregnancy, childhood, and adolescence (Abbaspour et al. 2014; Cashman 2002; Kabata-Pendias and Szteke 2015; Pohl et al. 2013).

Like many fresh fruits, medlar fruit is naturally rich in biogenic elements K, Ca, Mg, Na, P and Fe. Other nutritionally important elements such as S, Mn, Zn, Cu, Co, and Mo were also detected in the fruit. According to many studies K was detected as the most abundant element, followed by Ca, Mg and Na (Azizi 2011; Ercisli et al. 2012; Glew et al. 2007; Kalyoncu et al. 2013; Petö et al. 2016; Rop et al. 2011; Zołnierczyk et al. 2021). However, it was observed that the content of elements is influenced by the variety as well as the maturity stage of medlar fruit (Glew et al. 2007; Ercisli et al. 2012; Petö et al. 2016). Macroelements K, Ca and Mg especially showed clear decrease in the content during fruit maturation (Glew et al. 2007; Rop et al. 2011). Literature evidence suggests that medlar fruit can be considered a better source of some biogenic elements (K, Ca, Mg, P and Fe) compared to several other fruits such as apple, banana, grapes, mango, etc. (Ercisli et al. 2012). The elemental profile of medlar fruit and relevant analytical methods are presented in Table S1 (SI).

Phenolic compounds

Vitamins and essential elements are nutritive constituents of fruits that have a positive impact on human health, whereas phenolic compounds and carotenoids (lycopene, α- and β-carotene and xanthophylls) are non-nutritive plant constituents with benefits for human health (Kader 2002). Phenolic compounds are a distinctive class of bioactive compounds broadly distributed in nature. Polyphenols have been extensively studied over past decades, largely due to the association between consumption and their health benefits. Fruits as a remarkable source of phenolic compounds provide health benefits besides basic nutrition (Haminiuk et al. 2012). Various subclasses of polyphenols like flavonols, flavones, flavans, flavonones, coumarines and phenolic acids are present in medlar fruit (Figs. 4 and 5). Scarce literature points out the richness of medlar fruit in these bioactive compounds, Table 2 (Akbulut et al. 2016; Gruz et al. 2011; Gulcin et al. 2011; Katanić Stanković et al. 2022; Ozturk et al. 2019; Rop et al. 2011; Sadeghinejad et al. 2022; Tessa et al. 2021; Zołnierczyk et al. 2021). Most recently, isoflavonoid aesculetin (the simplest coumarin and aglycone metabolite of esculin) and flavonoid pinocembrin have been detected in the medlar fruits from Serbia (Katanić Stanković et al. 2022). Althought, the antioxidant activity of polyphenols is one of their most pronounced properties the role of polyphenolic compounds is recognized in many health issues such as cardiovascular disease, osteoporosis, neurogenerative disease, cancer, and diabetes mellitus. Flavonoids like quercetin, rutin, luteolin, quercetin-3-*O*-α-l-rhamnopyranoside, epicatechin gallate, etc., as well as some phenolic acids showed inhibitory activity against enzyme α-glucosidase responsible for carbohydrate digestion (AL-Ishaq et al. 2019; Assefa 2019; Isbilir et al. 2019).

Both benzoic acids (salycilic, protocatechuic, 3- and 4-hydroxybenzoic, *p*-aminobenzoic, syringic, gallic, etc.) and cinnamic acids (*p*-coumaric, chlorogenic, neochlorogenic, ferulic, caffeic, etc.) are found

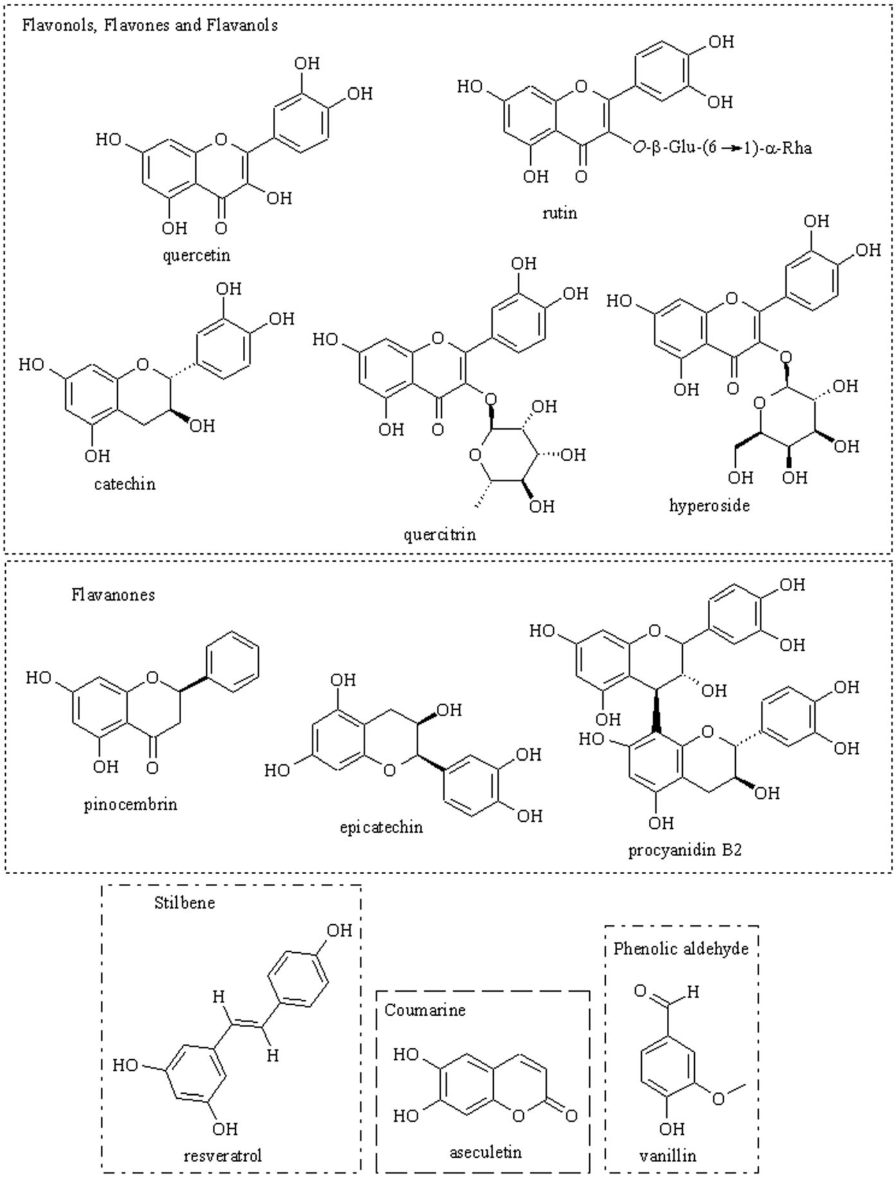


Fig. 4 Chemical structures of the most prominent phenolic compounds in medlar fruit

in medlar fruits, Table 2. Most phenolic acids are known to exert various bioactivies including: antifungal, antimutagenic, antimicrobial (4-hydroxybenzoic acid), anti-inflammatory, antipyretic, analgesic, antiseptic (salycilic acid), antihepatotoxic, anti-inflammatory, antioxidant, free radical scavenger, cytotoxic, chemopreventive, apoptotic, platelet aggregation inhibitory, neuroprotective, and LDL oxidation inhibitory (protocatechuic acid), antineoplastic, bacteriostatic, anti-tumor, antimelanogenic and antioxidant (gallic acid), antioxidant, antibacterial and hepatoprotective (syringic acid) (Khadem and Marles 2010). In several studies, cholorgenic acid was the most abundant among the detected phenolic acids (Akbulut et al. 2016; Katanić Stanković et al. 2022; Ozturk et al. 2019; Rop et al. 2011). It was observed that the concentrations of phenolic acids mostly decreased during the fruit ripening process (Gruz et al. 2011).

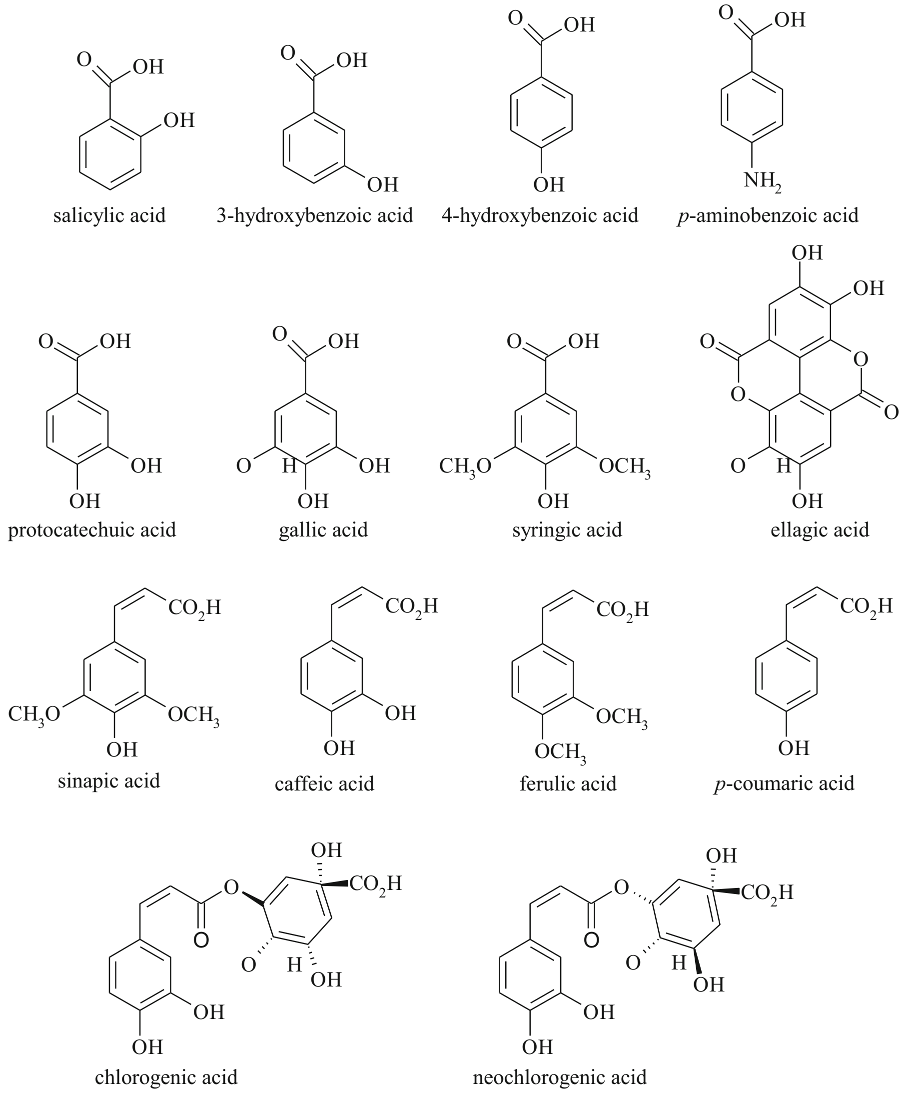


Fig. 5 Chemical structures of the most common phenolic acids in medlar fruit

Biological activity of medlar plant

Antioxidant activity

Many studies provided information about the antioxidant activity of different parts of the medlar plant (Table 3). Medlar fruit was found to be an effective antioxidant in several in vitro assays including DPPH (2,2-diphenyl-1-picrylhydrazyl), DMPD$^{\bullet+}$ (*N*,*N*-dimethyl-*p*-phenylenediamine), superoxide anion radicals scavenging activity, ferrous ion chelating activity, Fe^{3+}-Fe^{2+} reducing ability, CUPRAC (cupric ion reducing antioxidant capacity) (Gulcin et al. 2011; Katanić Stanković et al. 2022), β-carotene bleaching (Ercisli et al. 2012; Isbilir et al. 2019), ABTS (2,2-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (Secilmiş Canbay et al. 2015; Akbulut et al. 2016; Katanić Stanković et al. 2022), FRAP (ferric reducing antioxidant power) (Tessa et al. 2021) and TAC (total antioxidant capacity) assays (Katanić Stanković et al. 2022). Total antioxidant activity showed differences by genotypes (Akbulut et al. 2016; Cevahir and Bostan 2021; Ercisli et al. 2012). Moreover, extraction solvent also had an impact on the results obtained for antioxidant activity of medlar fruit. Methanol is reported to be a better solvent to extract antioxidants

Table 3 Antioxidant activity of the medlar plant (*M. germanica* L.)

Plant part	Extraction solvent	Assay	Result(s)	References
Fruits	Phosphate buffer	SOD enzyme activity	0.55	Campanella et al. (2003)
	Methanol	DPPH radical scavenging activity	Immature: ~ 80–100% Ripe: ~ 60–70% Overripe: ~ 20%	Gruz et al. (2011)
	Distilled water	DPPH, $DMPD^{\cdot +}$ and $O_2^{\cdot -}$ radicals scavenging activity, Fe^{2+} chelating activity, Fe^{3+}-Fe^{2+} reducing ability, FRAP, CUPRAC	0.36–2.76 µg TE	Gulcin et al. (2011)
	Methanol or water	DPPH, NO and H_2O_2 radicals scavenging activity, Fe^{2+} chelating activity	IC_{50} for methanol extract: 23–1138 µg/mL IC_{50} for water extract: 32–2333 µg/mL	Nabavi et al. (2011)
	HCl: methanol: water	ABTS radical scavenging activity	100–180 mg AAE/100 g	Rop et al. (2011)
	Acetone: water: acetic acid	β-carotene bleaching, DPPH radical scavenging activity	DPPH: 22–58 µg/mL β-carotene: 65–93%	Ercisli et al. (2012)
	Chloroform: methanol	ABTS radical scavenging activity	1.1 mmol TE/L	Secilmiş Canbay et al. (2015)
	Acetone: water: formic acid	DPPH radical scavenging activity	Controlled atmosphere: 4.65–94.33 mg/mg DPPH MAP: 4.65–93.37 mg/mg DPPH	Selcuk and Erkan (2015a)
			Control: 4.33–43.35 mg/mg DPPH 1-MCP treatment: 4.33–39.08 mg/mg DPPH	Selcuk and Erkan (2015b)
	HCl: methanol: water	ABTS radical scavenging activity	124–187 mg/100 g	Akbulut et al. (2016)
	Ethanol	DPPH radical scavenging activity, β-carotene bleaching	DPPH: 695 µg/mL β-carotene: 39.3%	Isbilir et al. (2019)
	Water	DPPH radical scavenging activity, FRAP	DPPH: ~ 100–150 mmol/kg TE (control) and ~ 140–150 mmol/kg TE (MAP) FRAP: ~ 120–220 mmol/kg TE (control) and ~ 100–220 mmol/kg TE (MAP)	Ozturk et al. (2019)

Table 3 continued

Plant part	Extraction solvent	Assay	Result(s)	References
Fruits	HCl: methanol: water	DPPH, FRAP, CUPRAC	Control: 14.74–126.16 µmol TE/g Microwave drying: 6.29–125.77 µmol TE/g Hot air drying: 6.51–125.77 µmol TE/g Vacuum drying: 6.30–98.40 µmol TE/g	Suna (2019)
	Water	DPPH radical scavenging activity	13.1–77.8 mmol TE/100 g	Cevahir and Bostan (2021)
	Aqueous methanol	FRAP	6.59 mmol Fe^{2+}/kg	Tessa et al. (2021)
	Ethanol: water: HCl	ABTS, FRAP	Fruit extract: 82.35–187.56 µM TE/g Methanol fraction: 137.13–245.31 µM TE/g Water fraction: 101.25–194.28 µM TE/g	Żołnierczyk et al. (2021)
	Water	DPPH, FRAP	Control: ~ 100–220 mmol TE/kg MAP or MAP + Aloe vera: ~ 135–220 mmol TE/kg	Ozturk et al. (2022)
	Ethanol	TAC DPPH· scavenging activity ABTS· + scavenging activity	238.2 ± 12.3 mg AAE/g IC_{50}: 884 ± 12 µg/mL IC_{50}: 2048 ± 144 µg/mL	Katanić Stanković et al. (2022)
Leaves	Methanol or water	DPPH, NO and H_2O_2 radicals scavenging activity, Fe^{2+} chelating activity	IC_{50} for methanol extract: 19–1129 µg/mL IC_{50} for water extract: 20–280 µg/mL	Nabavi et al. (2011)
	Ethanol	DPPH radical scavenging activity, β-carotene bleaching	DPPH: 400 µg/mL β-carotene: 73%	Isbilir et al. (2019)
	Methanol	DPPH radical scavenging activity	69.43%	Safari and Ahmady-Asbchin (2019)
Bark	Methanol or water	DPPH, NO and H_2O_2 radicals scavenging activity, Fe^{2+} chelating activity	IC_{50} for methanol extract: 11–427 µg/mL IC_{50} for water extract: 11–558 µg/mL	Nabavi et al. (2011)
Buds	Ethanol	DPPH radical scavenging activity, β-carotene bleaching	DPPH: 960 µg/mL β-carotene: 52%	Isbilir et al. (2019)

AAE Ascorbic acid equivalents; *ABTS* 2,2-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid); *CUPRAC* Cupric ion reducing antioxidant capacity; *DMPD*$^{\cdot+}$: *N*,*N*-dimethyl-*p*-phenylenediamine; *DPPH* 2,2-diphenyl-1-picrylhydrazyl; Fe^{2+}: ferrous ions; Fe^{3+}: ferric ions; *FRAP* Ferric reducing antioxidant power; H_2O_2: hydrogen peroxide; *MAP* Modified atmosphere packaging; *TAC* Total antioxidant capacity; *NO* Nitric oxide; $O_2^{\cdot-}$: superoxide anion; *SOD* Superoxide dismutase; *TE* Trolox® equivalent; 1-MCP: 1-methylcyclopropene compared to water (Nabavi et al. 2011). Similarly, Żołnierczyk et al. (2021) tested methanol and water fractions of freeze-dried medlar fruit and confirmed that the highest antioxidant activity was observed in the methanol extract.

It is important to consider the maturity stage of medlar fruit when evaluating its antioxidant potential. Accordingly, the antioxidant capacity of medlar fruit measured by the DPPH$^{\cdot}$ and ABTS$^{\cdot+}$ assays exhibited a decreasing trend during ripening (Gruz et al. 2011; Rop et al. 2011). Gruz et al. (2011) reported that the over-ripe medlar fruit had more than twice lower antioxidant capacity than the ripe fruit, which was harvested only 10 days later. Thus, medlar fruit should be consumed at the ripe maturity stage at the latest in order to provide higher health-promoting antioxidants. In the total antioxidant capacity assay 1 g of the medlar fruit extract showed equal activity as 238.2 mg of ascorbic acid. In the same test, the activity of the medlar fruit extract was significantly higher compared to the extracts of hawthorn and blackthorn fruits. On the other hand, in in vitro assays, medlar fruit showed lower antioxidant activity than blackthorn (Katanić Stanković et al. 2022). In another study, measuring the relative antioxidant activity of medlar fruit with SOD (superoxide dismutase) enzyme assay revealed that medlar fruit possesses higher antioxidant capacity than apples, apricots, bananas, cherries, figs, grapes, melons, peaches, pears, pineapples, plums, and watermelons (Campanella et al. 2003).

Several studies have explored the effect of different storage conditions on the antioxidant activity of medlar fruit. Selcuk and Erkan (2015a) found that the antioxidant activity, as measured by the DPPH scavenging assay was higher in fruits stored in a modified atmosphere packaging system compared to those stored in a controlled atmosphere. However, the antioxidant activity decreased during 60 days of storage. The same research group (Selcuk and Erkan 2015b) further investigated the effect of 1-MCP (1-methylcyclopropene) treatment on antioxidant activity of medlar fruits during long-term storage in the palliflex storage system. The results showed that 1-MCP treatment helped the medlar fruits maintain a high level of antioxidant activity, which gradually decreased during storage. In another study, loss of antioxidant activity was significantly delayed during the storage of medlar fruits by applying modified atmosphere packaging alone or in combination with methyl jasmonate (Ozturk et al. 2019). Similarly, modified atmosphere packaging alone or in combination with Aloe vera gel resulted in higher retention of antioxidant capacity during storage (Ozturk et al. 2022).

Suna (2019) investigated the effect of different drying treatments including microwave, hot air and vacuum drying on the antioxidant capacity of medlar fruit using DPPH, CUPRAC and FRAP assays. The results revealed that all drying methods reduced the antioxidant capacity (0.3–57%), where microwave drying gave the best results in terms of antioxidant retention. The author further examined the effect of in vitro gastrointestinal digestion on the antioxidant capacity of the dried medlar fruits. Bioaccessibility of antioxidants after digestion varied. According to the results of DPPH and FRAP assays, the antioxidant capacity of the dried medlar fruits was enhanced after digestion. On the other hand, CUPRAC assay results were contradictory to these findings. It is well known from the literature that the measurement of antioxidant capacity cannot be evaluated successfully with a single assay. Therefore, it is highly recommended to employ a variety of assays with different mechanisms in order to obtain a more comprehensive understanding (Capanoglu et al. 2018).

Aside from investigating the fruit, a few studies have also examined the antioxidant capacity of medlar leaves, bark and buds. Safari and Ahmady-Asbchin (2019) measured the DPPH radical scavenging activity of medlar leaves reported that dried leaves possessed strong antioxidant properties. Nabavi et al. (2011) compared the antioxidant capacity of medlar fruit, bark and leaf and concluded that bark extracts possessed the highest antioxidant among the tested samples. The authors also found that the radical scavenging activity of all extracts increased with increasing concentration. Similarly, Isbilir et al. (2019) assessed the antioxidant capacity of different parts of medlar including fruit, leaf and flower bud using DPPH and β-carotene bleaching assays. For both assays, leaf extract showed the strongest antioxidant activity followed by flower buds and fruits.

Antimicrobial activity

The studies reporting the antimicrobial activities of the medlar plant are quite limited (Table 4). Niu et al.

Table 4 Antimicrobial activity of the medlar plant (*M. germanica* L.)

Plant part	Extraction solvent	Assay	Result(s)	References
Fruits	Water or ethanol	Disc diffusion method against *Staphylococcus aureus* and *Klebsiella pneumoniae*	Water extract: MIC: 2.5–5 mg/mL; MBC: 50–100 mg/mL Ethanol extract: MIC: 0.625–2.5 mg/mL; MBC: 2.5–50 mg/mL	Niu et al. (2013)
	Water or ethanol	Disc diffusion methods against *Streptococcus pyogene*, *Listeria innocua*, *Enterobacter aerogenes* and *Klebsiella pneumoniae*	Water extract: MIC: 4–64 mg/mL; MBC: 8–128 mg/mL Ethanol extract: MIC: 2–32 mg/mL; MBC: 4–64 mg/mL	Tabatabaei-Yazdi et al. (2015)
	Ethanol, methanol, acetone or water	Disc diffusion method against *Escherichia coli, Staphylococcus aureus*, *Listeria monocytogenes*, *S. enterica* ser. Typhimurium, *Bacillus cereus, Shigella dysenteria, Aspergillus flavus, Aspergillus niger, Penicillium notatum, Penicillium crysogenum, Mucor racemosus* and *Rhizopus nigricans*	Ethanol extract: MIC: 70.31–562.5 µg/mL; MBC: 46.88–375 µg/mL Methanol extract: MIC:187.5–1500 µg/mL; MBC: 187.5–1000 µg/mL Acetone extract: MIC: 93.75–500 µg/mL; MBC: 46.88–1000 µg/mL Water extract: MIC: 23.43–140.63 µg/mL; MBC: 11.72–125 µg/mL	Denizkara et al. (2021)
Leaves	Water	Disc diffusion method against *Staphyloocus aureus*, *Escherichia coli*, *Proteus mirabilis* and *Pseudomonas aeruginosa*	Inhibition zones: 7–17 mm	Bouabdelli et al. (2012)
	Methanol or ethanol	Disc diffusion method against *Pseudomonas aeruginosa, Staphylococcus aureus* and *Escherichia coli*	Methanol extract: MIC: 63–250 mg/mL Ethanol extract: MIC: 0–500 mg/mL	Ahmady-Asbchin et al. (2013)
	Aqueous acetone	Disc diffusion method against *Klebsiella pneumoniae*, *Vibrio cholera*, *Escherichia coli* and *Shigella dysenteriae*	MIC: 3.333–6.667 mg/mL; MBC: 5.833–9.167 mg/mL	Davoodi et al. (2017)
	Methanol	Disc diffusion method against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Salmonella typhi*, *Salmonella paratyphi*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, *Enterococcus faecalis*, *Yersinia enterocolitica*, *Serratia marcescens*, *Shigella dysenteriae* and *Citrobacter freundii*	MIC: 62.5–125 mg/mL	Safari and Ahmady-Asbchin (2019)

MBC Minimal bactericidal concentration; *MFC* Minimum fungicidal concentration; *MIC* Minimal inhibitory concentration

(2013) examined the antibacterial effect of medlar fruits against two pathogenic bacteria: *Staphylococcus aureus* and *Klebsiella pneumoniae*. The authors found that the medlar fruit extracts were moderately sensitive to *Staphylococcus aureus*, whereas its inhibiting effect on *Klebsiella pneumoniae* was particularly significant. Moreover, the medlar fruit extract prepared with ethanol possessed better antibacterial activity compared to the water extract. Similarly, Tabatabaei-Yazdi et al. (2015) also investigated the effect of medlar fruit extract on the growth of *Streptococcus pyogene*, *Listeria innocua*, *Enterobacter aerogenes* and *Klebsiella pneumoniae.* The extracts showed more effective antibacterial impact on the growth of *Streptococcus pyogene* and *Listeria innocua* compared to *Enterobacter aerogenes* and *Klebsiella pneumoniae,* indicating that the medlar fruit extract possessed a higher antibacterial effect on Gram-positive bacteria compared to Gram-negative bacteria. Moreover, when compared to common therapeutic antibiotics, medlar fruit extract had higher inhibitory effect on some of the studied strains. A recent study by Denizkara et al. (2021) assessed the antibacterial and antifungal effects of medlar fruit extracts prepared with different solvents including ethanol, methanol, acetone, and water. Disc diffusion method was employed to test the activity of prepared extracts against *Escherichia coli, Staphylococcus aureus*, *Listeria monocytogenes*, *S. enterica* ser. Typhimurium, *Bacillus cereus, Shigella dysenteria, Aspergillus flavus, Aspergillus niger, Penicillium notatum, Penicillium crysogenum, Mucor racemosus* and *Rhizopus nigricans*. The results revealed water extracts as the samples showing the strongest antimicrobial effects.

Several studies have investigated the antimicrobial effects of medlar leaves. Bouabdelli et al. (2012) prepared 4 different water extractions including infusion, decoction, maceration and percolation from medlar leaves and tested their antimicrobial effect against *Staphylooccus aureus*, *Escherichia coli*, *Proteus mirabilis* and *Pseudomonas aeruginosa.* The results showed that the infusion and decoction of medlar leaves exhibited good antibacterial activity. In another study (Ahmady-Asbchin et al. 2013), the antibacterial effects of methanolic and ethanolic extracts of medlar leaves were evaluated against *Pseudomonas aeruginosa, Staphylococcus aureus* and *Escherichia coli*, which were isolated from hospital environments. The growth inhibition of all bacteria was greater for methanolic leaf extracts compared to ethanolic leaf extracts. Similarly, Davoodi et al. (2017) assessed the antibacterial activity of hydro-acetonic extracts of medlar leaves against *Klebsiella pneumoniae*, *Vibrio cholera*, *Escherichia coli* and *Shigella dysenteriae* and found that the extract exhibited the best inhibitory and bactericidal activities against *Klebsiella pneumoniae.* In a more recent study (Safari and Ahmady-Asbchin 2019), the antibacterial activity of different concentrations of methanolic extract of medlar leaves was evaluated against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Salmonella typhi*, *Salmonella paratyphi*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, *Enterococcus faecalis*, *Yersinia enterocolitica*, *Serratia marcescens*, *Shigella dysenteriae* and *Citrobacter freundii*. The highest inhibition activity was observed against *Staphylococcus aureus.* In general, medlar leaf extracts showed higher antibacterial activity against Gram-positive bacteria compared to Gram-negative bacteria. Moreover, the antibacterial effect of medlar leaf extract against certain bacteria including *Staphylococcus aureus, Staphylococcus epidermidis* and *Escherichia coli* was stronger than that of the tested antibiotic, gentamicin.

Antidiabetic activity

Diabetes mellitus, commonly known as diabetes, is a major public health concern worldwide. α-Amylase and α-glucosidase are the main enzymes for the treatment of diabetes. Antidiabetic agents such as dietary polyphenols are also key strategies in combating the disease. However, limited studies have been conducted on the antidiabetic activity of different parts of the medlar plant as seen in Tables 5 and 6. A recent study showed that ethanolic extract of medlar fruit expressed inhibitory activity toward α-glucosidase in an in vitro assay, surpassing the standard antidiabetic drug acarbose (Katanić Stanković et al. 2022). Isbilir et al. (2019) investigated the α-amylase and α-glucosidase enzyme inhibitory effects of different parts of the medlar plant including the fruit, leaf and flower bud. All medlar extracts showed inhibitory activity against α-glucosidase whereas the fruit and bud extracts inhibited porcine pancreatic α-amylase. Among the studied extracts, the bud extract showed

Table 5 Antidiabetic activity of the medlar plant (*M. germanica* L.)

Plant part	Extraction solvent	Assay	Result	References
Fruit	Ethanol	α-glucosidase inhibition	Extract showed the potent inhibitory activity with an IC_{50} value of 199.84 µg/mL when compared with the activity of the standard drug acarbose (IC_{50} 201.38 µg/mL)	Katanić Stanković et al. (2022)
Fruit, leaf and flower bud	Ethanol	α-amylase and α-glucosidase inhibition	The bud and fruit extract of medlar showed inhibition activity against α-amylase and α-glucosidase, but the leaf extract only showed inhibitory activity toward α-glucosidase	Isbilir et al. (2019)
Fruit	Methanol water	α-amylase inhibition	Both fractions showed positive antidiabetic effects The percentage of α-amylase inhibition values of the 1, 5, 10, and 20 mg/mL DMSO were 35, 52, 79, and 100%, respectively	Żołnierczyk et al. (2021)

the highest inhibitory activity against the α-amylase and α-glucosidase. The authors reported that the inhibitory effect could be attributed to the phenolic acids of the medlar plant. This result is in accordance with Żołnierczyk et al. (2021), who observed that the medlar extract, methanolic fraction and water fraction, showed antidiabetic effects. Among different concentrations of the medlar extracts, a small concentration of the water fraction showed the highest antidiabetic effects. The percentage of α-amylase inhibition values of the 1, 5, 10, and 20 mg/mL DMSO were 35, 52, 79, and 100%, respectively. Kouhestani et al. (2018) investigated the effects of the flavonoid fraction of *M. germanica* leaves on metabolic syndrome in ovariectomized rats. They reported that the treatment with the flavonoid fraction of *M. germanica* leaves significantly reduced the serum level of insulin, glucose, and TNF-α. In another study, Shafiee et al. (2018) assessed the effect of *M. germanica* leaf extract on serum glucose lowering, antioxidative stress effects, and normalization of animal body weight in normal and streptozotocin-induced Balb/C mice. Oral administrations of the *M. germanica* leaf extract significantly reduced oxidative stress, serum glucose, and lipid peroxidation and maintained animal body weight during the treatment period ($p < 0.05$) compared to metformin (200 mg/kg) in Balb/C diabetic mice. A more recent study by Aşkar et al. (2022) investigated the effects of the medlar plant on glucose metabolism, and apoptotic markers in diabetic rats. The study found that the diabetic rats treated with the medlar had significantly lower serum glucose, caspase-3, and caspase-8 levels compared to the diabetic group.

Other biological activities

Different biological activities of the medlar are given in Table 6. Cytotoxic activity of medlar fruit extract was examined on three human tumor cell lines: cervical adenocarcinoma (HeLa), melanoma cell line (FemX) and colorectal adenocarcinoma (LS-174 T). Medlar fruit extract showed the strongest cytotoxic activity against HeLa cells with an IC_{50} value of 624.83 µg/mL. The extract also showed weak activity toward FemX cells with IC_{50} values 854.98 µg/mL, whereas no cytotoxic activity against LS-174-T cells was observed (Katanić Stanković et al. 2022). Hoseinifar et al. (2017) investigated the effects of dietary medlar leaf extract on the growth performance, skin mucus non-specific immune parameters, and antioxidant related genes in the skin of common carp fingerlings. Medlar leaf extract improved growth performance in fingerlings, regardless of the inclusion level. Moreover, the administration of medlar leaf extract raised the expression of antioxidant enzymes gene expression in the skin. In a separate study, Darbandi et al. examined the effects of *M. germanica* leaf extract on cognitive performance, learning and memory function in an intra-cerebroventricular streptozotocin-induced Alzheimer's disease model in male Wistar rats. They found that the injection of streptozotocin significantly reduced cognitive function, memory retention as well as CA1 intact neurons compared to the control group, while the flavonoid extract of the medlar considerably improved cognitive functions and memory retention. In addition, the number of intact cells in hippocampal CA1 area

Table 6 Preclinical studies of the medlar plant (*M. germanica* L.)

Biological function	Plant part	Subject	Model	Dose	Duration	Results	References
Antidiabetic activity	Leaves	Twenty-four adult female Wistar rats	Ovariectomized Rats	Intraperitoneal injection 10 mg/kg	3 weeks	The flavonoid fraction- reduced serum level of insulin, glucose, and TNF-α	Kouhestani et al. (2018)
	Leaf	Forty-eight matured male Balb/C mice	Intraperitoneal injection of Streptozotocin (35 mg/kg)	Oral administrations: 50, 100, and 200 mg/kg body	3 weeks	The leaf extract significantly decreased serum glucose and maintained normal body weight in Balb/C diabetic mice	Shafiee et al. (2018)
		Twenty-eight male Sprague–Dawley rats	Intraperitoneal of Streptozotocin (65 mg/kg)	Oral administrations: 100 mg/kg	4 weeks	Medlar supplementation decreased serum glucose, caspase-3, and caspase-8 levels	Aşkar et al. (2022)
Cytotoxic activity	Fruit	Human tumor cell lines: cervical adenocarcinoma (HeLa), melanoma cell line (FemX) and colorectal adenocarcinoma (LS-174 T)	–	Extracts and fractions ranging from 1000 to 62.5 µg/mL	–	Medlar fruit extract showed the strongest cytotoxic activity on HeLa cells with an IC_{50} value of 624.83 µg/mL The extract showed weak activity toward FemX cells with IC_{50} value of 854.98 µg/mL, whereas no cytotoxic activity against LS-174-T cells was shown	Katanić Stanković et al. (2022)
Neurodegenerative activity	Leaves	Male Wistar rats	Intracerebroventricular streptozotocin-induced Alzheimer's disease	Infuses of 5, 10 and 20 mg/kg	3 weeks	The extract improved cognitive functions and memory retention	Darbandi et al. (2018)
	Leaves	Forty-eight male Wistar rats	Amyloid beta-treated-injected rat	Treatment: 5, 7.5 and 10 mg/kg	3 weeks	The extract improved amyloid beta-42 induced memory dysfunction	Davoudzadeh et al. (2018)
Skin mucosal immunity	Leaf	Fifteen fish	–	Diets supplemented with graded levels (0, 0.25, 0.50, and 1.00%) of the extract	7 weeks	Medlar leaf extract improved growth performance in fingerlings, regardless of the inclusion level. Administration of medlar leaf extract raised the expression of antioxidant enzymes gene expression in skin	Hoseinifar et al. (2017)

IC_{50} (µg/mL): Concentrations of examined extracts inducing a 50% decrease in cells survival rate gradually increased and the number of dead cells decreased. Conversely, Davoudzadeh et al. (2018) reported that the flavonoid extract of the medlar leaves could improve amyloid beta-42 induced memory dysfunction in rats, partially due to its role in reducing cytochrome c levels.

Conclusion

M. germanica L. is becoming increasingly popular due to the unique attributes of its fruits; even though it is considered a neglected species. The fruits are edible throughout the winter because they can be stored in an ordinary warehouse for a few months, and even longer in refrigerators. When rotted or frozen, the fruits become soft, sweet, and juicy. Scientific papers have revealed significant amounts of sugars, organic acids, carotenoids, vitamins, essential elements and, polyphenol compounds in medlar fruits. Different parts of the plant including the fruits, leaves, bark, and bud flowers are used in traditional medicine for treating various diseases or medical conditions. However, there is a scarcity of comprehensive literature on the chemical composition and biological properties of the medlar plant and clinical studies are lacking. Therefore, further studies, particularly on the flavonoids of the plant, need to be conducted. This review highlights the potential of the fruit as a good natural source of bioactive compounds offering the possibility of its application in gastronomy, and the food industry for the development of new products and value-added foods. Knowledge about the nutritional, chemical and pharmacological properties of medlar fruits is essential to regain attention to this exceptional fruit tree and to restore its cultivation and consumption.

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Declarations

Conflict of interest The authors declare they have no conflicts of interest.

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