



Eriobotrya japonica (Thunb.) Lindl.: Ethnomedicinal uses, phytochemical contents and pharmacological properties: A Review

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Review

Abstract

Background: *Eriobotrya japonica* (Thunb.) Lindl. (*E. japonica*) is a small evergreen tree, commonly called loquat, that belongs to the Rosaceae family. It is widespread in Asia, Mediterranean region and on the American continents. Depending on its origin and source, loquat is divided into two main types Chinese loquat and Japanese loquat and many varieties have been developed from them. Although no authentic data is available on its global production, in 2019, it was estimated to be around 1.58 million tons. This review highlights the morphology, ecology, ethnomedicinal uses, phytochemical constituents and biological activities of *E. japonica*.

Methods: Extensive literature searches were carried out using scientific databases like Scopus, ScienceDirect, Springer, Web of Science, JSTOR, PubMed and Google Scholar.

Results: Different parts of this plant (leaves, fruit, bark, stem, flowers and roots) are used in folk medicine to treat respiratory disorders, diabetes, kidney illnesses and cardiovascular problems. *E. japonica* is a rich source of many bioactive components such as polyphenols, flavonoids, terpenoids, carotenoids, minerals, vitamins and dietary fibers. These bioactive compounds act as antioxidant, anti-inflammatory, antidiabetic, cardioprotective, anticancer, antidiarrheal and hepatoprotective and are considered for its pharmacological effects. Studies on animals have shown that various parts of loquat and their aqueous extracts are not toxic even at high doses (aqueous extracts of loquat leaves (LLE) at 5000 mg/kg BW).

Conclusions: This review comprehensively summarizes the botany, ecology, phytochemistry, and biological activities of *E. japonica*. It also provides some practical provision for future research on this plant.

Keywords: Loquat; *Eriobotrya japonica*; Rosaceae; Ethnomedicinal uses; Phytochemistry; Pharmacology; Toxicity

Background

Loquat (*Eriobotrya japonica* (Thunb.) Lindl.) is an economically important subtropical fruit tree of the Rosaceae family, which is native to China. It is also named as *Mespilus japonica*, *Photinia japonica*, *Folium eriobotryae*. Although no authentic data is available on its global production, in 2019, it was estimated to be around 1.58 million tons (Singh *et al.* 2023). Loquat fruit has a high market value. However, it is highly perishable and is susceptible to rotting due to humidity. As a result, nutritional losses occur after the harvest. The color of the loquat flesh allows us to distinguish between its two varieties: red-fleshed and bench-fleshed loquats, the first is rich in carotenoids, while the other is rich in glutamic acid (Baljinder *et al.* 2010, Dhiman *et al.* 2022). Locally, *Eriobotrya japonica* is known as loquat or Japanese plum in English, beshmelah in Arabic, and bibassier or néflier du Japon in French (Ibrahim 2021, Lim 2012). The fruit of *E. japonica* is rich in dietary fiber and contains high amounts of vitamin A, ascorbic acid and many essential minerals (Dhiman *et al.* 2022). It is also characterized by the presence of triterpenes, flavonoids, sesquiterpene glycosides, megastigmane derivatives, phenylpropanoids, organic acids, and volatile oils, which explains its health benefits (Zhu *et al.* 2022). Different plant parts are being used in traditional medicine to treat many diseases including diabetes, respiratory disorders, cardiovascular diseases and digestive disorders (Banno *et al.* 2005, Fakchich & Elachouri 2014). Beyond its medicinal properties, loquat is also widely used in culinary and industrial applications (Kumar *et al.* 2024, Selvamuthukumaran *et al.* 2020).

E. japonica exhibits various pharmacological activities (Savaliram & Rahul 2024), including antioxidant (Zhou *et al.* 2011), antidiabetic (Khouya *et al.* 2022), cardioprotective (Huang *et al.* 2022), antitumor (Hsieh *et al.* 2021), and hepatoprotective (Shahat *et al.* 2018) properties. Its neuroprotective (Shirvani *et al.* 2017) and anti-inflammatory (Kuraoka-Oliveira *et al.* 2020) effects have also been demonstrated. Additionally, some studies have also reported its bronchodilatory (Marianne *et al.* 2021), hypoglycemic and hypolipidemic effects (Abdelrahman *et al.* 2023, Mokhtari *et al.* 2023, Mokhtari *et al.* 2024).

The loquat is distinguished by its rich bioactive compounds, which contribute to its multiple biological activities. Among these, nerolidol derivatives, such as nerolidol-3-O- α -L-rhamnopyranosyl-(1-4)- α -L-rhamnopyranosyl-(1-2)-[α -L-rhamnopyranosyl-(1-6)]- β -D-glucopyranoside, extracted from its leaves, have shown antidiabetic effects (Li *et al.* 2020b). Furthermore, sesquiterpene glycosides obtained from the leaves exhibit significant antioxidant and hepatoprotective properties (Jian *et al.* 2017). Additionally, several megastigmane glycosides, including (6S,9R)-roseoside and eriojaposide A, isolated from the leaves, have demonstrated antitumor activity (Ito *et al.* 2002). Moreover, epicatechin extracted from loquat leaves possesses antimicrobial properties (Bae *et al.* 2005), while methyl ursolate exerts a potent anti-inflammatory effect (Banno *et al.* 2005). Finally, several other bioactive compounds extracted from the leaves, such as euscaphic acid, 1 β -hydroxyeuscaphic acid, procyanidin B-2, and roseoside, have exhibited significant anticancer activity (Banno *et al.* 2005, Ito *et al.* 2002). Additionally, tormentic acid, isolated from the plant's suspension cultures, has demonstrated a notable hepatoprotective effect (Jiang *et al.* 2017).

This review offers a comprehensive analysis of the botany, ecology, traditional medicinal uses, phytochemistry, pharmacology, and toxicology of *E. japonica*. Additionally, it provides key insights to guide future research on this plant.

Materials and Methods

The aim of this review is to collect, analyze and summarize all research targeting the morphology, ecology, ethnomedicine, pharmacology and toxicology of the *E. japonica* plant. The data presented in this study were systematically collected from scientific databases, including Scopus (<https://www.scopus.com/>), ScienceDirect (<http://www.sciencedirect.com/>), Springer (<https://link.springer.com/>), Web of Science (<https://www.webofknowledge.com/>), JSTOR (<https://www.jstor.org/>), PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/>) and Google Scholar (<https://scholar.google.com/>). The search terms used were the scientific name of the plant "*Eriobotrya japonica*" or its common name "loquat" followed by "and", followed by the requested field "Ethnobotany or toxicology". The results obtained were filtered based on title, keywords and abstract. The references section contains 206 references, including original research articles, review papers, books, sections of books, and conference proceedings. Strict inclusion and exclusion criteria were applied to ensure the relevance and scientific quality of the studies analyzed. Only peer-reviewed publications indexed in recognized databases, such as PubMed, Scopus, and Web of Science, were included, most of which are written in English. Recent studies published between 2000 and 2025 were prioritized to reflect the current state of knowledge. Conversely, unpublished research, such as theses and reports, as well as studies from non-indexed and non-peer-reviewed journals, were excluded. This methodological approach ensures a rigorous and reliable review, enabling conclusions to be drawn based on solid scientific evidence. Additionally, chemical structures were drawn using ChemDraw Professional 15.0 software and verified through PubChem (<https://pubchem.ncbi.nlm.nih.gov/>).

Results

Origin and distribution

Loquat is a fruit tree cultivated in China since more than 2000 years and its origin is Chinese (Li *et al.* 2016). It was subsequently implanted in Japan from China and took the name *japonica*, whose traces have been observed since 1180 (Gisbert *et al.* 2009). Thunberg (1784) considered Japan as the main origin of loquat, therefore he named it as *Mespilus japonica* Thunb. Other authors have considered China and Japan together as the origin of the species *E. japonica* (Lin *et al.* 1999). According to Badenes *et al.* (2009) the southeast of the Gongga Mountains, the lower and middle region of the Dahube River were the main centers of origin of loquat, thus the Yunnan region was the second center. In the 18th century, the loquat was introduced to Europe as an ornamental plant in botanical gardens (Caballero & Fernández-Zamudio 2004, Martínez-Calvo *et al.* 2000). Currently *E. japonica* is widely distributed throughout the world in more than 30 countries including Asian continent, the Mediterranean region and the American continent (De Almeida Lopes *et al.* 2018, Jiang *et al.* 2022) (Fig. 1). In 1960, loquat was introduced to Morocco for its cultivation. This species is found in several areas of Morocco, especially in the Zegzel Valley in the east of the country (El Marouani *et al.* 2020, Kabiri *et al.* 2023).

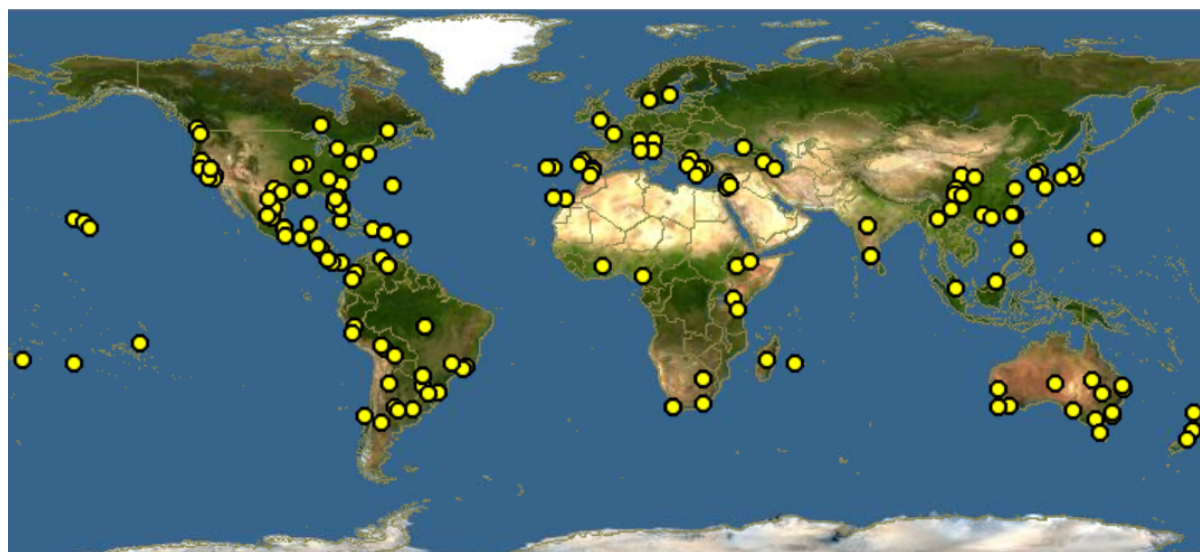


Figure 1. A map illustrating the global distribution of *E. japonica* (Zhu *et al.* 2022).

Agroecology

The species *E. japonica* is well adapted to the subtropical to temperate climate, as well as to the Mediterranean climate where it grows in the same habitat as the citrus species (Badenes *et al.* 2000, Lim 2012). However, with certain ecological constraints, the development cycle of flowers and fruits lengthens during the winter season, which is because the average temperature is higher than 15°C. The wind and frost can destroy the fruits, as the drop in temperature can damage the open flowers and the fruits (Caballero & Fernández-Zamudio 2004). Loquat can grow on a wide range of soils of moderate fertility (clay-sandy, also oolitic limestone), requiring good drainage, with a pH between 0 and 8. Its roots are sensitive to salinity and can suffocate (Lim 2012, Martínez-Calvo *et al.* 2000). *E. japonica* is present in regions at latitudes ranging from 20 and 35° north or south, but it could also be cultivated in areas located at 45° latitude in a maritime climate (Jiang *et al.* 2022, Lin *et al.* 1999). The most suitable directions for its cultivation are the southeast or the south (in the northern hemisphere), at an altitude of < 400 m. This species could also be grown without additional irrigation when rainfall exceeds 1200 mm (Martínez-Calvo *et al.* 2000).

Taxonomy and classification

Loquat was first described by the Swedish botanist Thunberg in 1784 and was placed in the genus *Mespilus*. Subsequently in 1822 it was revised by the English botanist John Lindley who deposited it in the genus *Eriobotrya* that is derived from the Greek words "*erion*" that means wool and "*botrys*", which means clusters because of the woolly and grouped appearance of the panicles. The species name *japonica* came from Thunberg's belief that the loquat was of Japanese origin. *Eriobotrya* belongs to the Rosaceae family and the Maloideae as subfamily (Jiang *et al.* 2022, Lin *et al.* 1999, Martínez-Calvo *et al.* 2000, Sultan 2017).

The number of species in the genus *Eriobotrya* differ among scientists around the world. According to Dhiman *et al.* (2022), Sagar *et al.* (2020) seventeen species of loquat have been identified. Only *E. japonica* is cultivated for fruit production while *E. deflexa* and *E. prinoides* are used for rootstocks (Dhiman *et al.* 2022, Sultan 2017). From a botanical point of view and depending on their origin, we distinguish two types of loquats: “Chinese” and “Japanese”. The Chinese group is characterized by thin leaves, large pear-shaped to round fruits with yellow peel and flesh and numerous seeds. The Japanese group is distinguished by broad leaves, small pear-shaped to oblong fruits with light yellow or white peel and flesh with a single seed or a few large seeds (Badenes *et al.* 2000, Dhiman *et al.* 2022, Martínez-Calvo *et al.* 2000, Sagar *et al.* 2020, Sultan 2017). Currently a large number of loquat varieties have been developed from these two types through natural hybridization and artificial mutation techniques (Martínez-Calvo *et al.* 2000, Sultan 2017).

Botanical description

E. japonica is a small evergreen tree or shrub, which is up to 10 m tall, with a gray-brownish, smooth straight and short trunk. The leaves are simple and large with a length of 12 to 30 cm and a width of 3 to 9 cm, alternate, elliptical or obovate-oblong in format, thick, leathery, serrated at the top, with short petioles. Their upper sides are shiny dark green, while their lower sides are gray with a cottony appearance. Leaf fall does not have a defined period. The flowers are numerous (30 to 100 flowers), small, 1.2 to 2 cm in diameter, white or yellowish white. They are bisexual and are very fragrant in winter and are collected in terminal panicles (clusters). Each flower is composed of a calyx of five fused, triangular and persistent sepals, a corolla of five free white or cream petals, orbicular or obovate in shape, 10 to 40 stamens, two to five styles, an inferior ovary attached to the calyx consisting of three to five fused carpels with two ovules per cell. The loquat blooms in early winter or fall (October to February). The fruits ripen in late spring and early summer (April to early June). The loquat is yellow or orange-yellow, round, oval or elliptical, and weighs 30 to 55 g, with a length of 3 to 4 cm and a width of 2 to 5 cm. They are arranged in clusters of 4 to 30 fruits. The fruit is composed of a pulp with a flavour ranging from sweet to sour depending on the variety and stage of maturation coated in a yellow-orange peel and three to five brown seeds located in the center of the fruit. The loquat is characterized by a superficial root system reaching 25-30 cm in depth (De Almeida Lopes *et al.* 2018, Ibrahim 2021, Li *et al.* 2016, Lim 2012, Lin *et al.* 1999, Martínez-Calvo *et al.* 2000, Sultan 2017). Fig. 2 shows photos of *E. japonica*.

Production

The statistical data on loquat production is unavailable on the website of the Food and Agriculture Organization of the United Nations (FAOSTAT). There is no authentic data available on the global production of loquat. However, it is estimated that its current global production is around 1.58 million tons (Singh *et al.* 2023). These values have been collected from the published journal articles and scientific reports from the various loquat producing countries. Today the loquat is globally produced in several countries. Asia and the Mediterranean region are the main producing areas. In 2019 and 2020, the world production of loquat was estimated to be 994698 tons, of which China was the first producing country with a production of 919000 tons representing 93.6% of the total production followed by Spain which is the first country that exported loquat in the world with a production of 28836 tons and an export of 18160 tons (Jiang *et al.* 2022). China, Spain, Turkey, Italy, Japan, India and Pakistan are the main loquat producing countries (Jiang *et al.* 2022, Singh *et al.* 2023). Table 1 lists countries with conventional loquat planting areas exceeding 30 hectares. Greece has been reported to have 300 ha area with a production of 2750 tons (Caballero & Fernández-Zamudio 2004). According to the estimates presented by Khan (2003) loquat is cultivated in Pakistan on about 10000 ha of land with a total production of 128000 tons, but is not of export quality (Abbasi *et al.* 2010).

At the beginning of the last century, the loquat cultivation started in Morocco when it was brought from Algeria by French colonization (Kodad *et al.* 2023). According to Caballero and Fernández-Zamudio (2004), the Moulouya region located in the north-west of Morocco represents 80% of the areas planted with loquat, with a total production of 6400 tons of which Musca, Navela, Mkarkeb, Tanaka and Argelino are the main cultivated varieties. The Zegzel valley located in the eastern region of Morocco represents 85% of the national loquat cultivation areas. In 2021, the national production of loquat in Morocco exceeded 10000 tons (Kodad *et al.* 2023).



Figure 2. *E. japonica* tree (a), its leaves (b) and fruits (c) (photo by N. El-aouni in the region of Oujda city, Morocco).

Table 1. Area and production loquat in the major producing countries.

Country	Area (ha)	Production (tons)	Total production (%)	Reference
China	157400	919000	86.47	(Jiang <i>et al.</i> 2022)
India	7300	44000	4.14	(Singh <i>et al.</i> 2023)
Spain	2914	41487	3.90	(Caballero & Fernández-Zamudio 2004)
Turkey	809	16402	1.54	(Jiang <i>et al.</i> 2022)
Pakistan	10000	12800	1.20	(Caballero & Fernández-Zamudio 2004)
Japan	2420	10245	0.96	
Morocco	385	6400	0.60	
Italy	453	5918	0.56	(Jiang <i>et al.</i> 2022)
Greece	300	2750	0.26	(Caballero & Fernández-Zamudio 2004)
Brazil	300	2400	0.23	
Portugal	243	950	0.09	
Chile	32	220	0.02	
Cyprus	30	185	0.02	(Jiang <i>et al.</i> 2022)

The uses of *E. japonica*

Ethnomedicinal uses

Loquat is traditionally used to treat respiratory disorders in many countries such as Morocco (Merrouni *et al.* 2021, Merzouki *et al.* 2000), Libya (El-Mokasabi *et al.* 2018), Madagascar (Paniagua-Zambrana *et al.* 2020), Kenya (Odongo *et al.* 2018), Turkey (Akaydin *et al.* 2013, Gürdal & Öztürk 2022), Italy (Menale *et al.* 2016), Mexico (Andrade-Cetto 2009), Ecuador (Tene *et al.* 2007), China (Banno *et al.* 2005, Hu *et al.* 2020, Li *et al.* 2016, Lu *et al.* 2022, Xiong *et al.* 2020), Pakistan (Azeem *et al.* 2020) and India (Kumar *et al.* 2021, Kumar & Duggal 2019). It is also used against digestive disorders in Morocco (Bellakhdar *et al.*

1991, Ben Akka *et al.* 2019, Fakchich & Elachouri 2014, Merrouni *et al.* 2021, Ziyyat *et al.* 1997), Kenya (Odongo *et al.* 2018), Turkey (Akaydin *et al.* 2013), Portugal (Novais *et al.* 2004), Spain (Benítez *et al.* 2010), Italy (Menale *et al.* 2016), Ecuador (Bussmann 2002, Tene *et al.* 2007), China (Hu *et al.* 2020), Japan (Banno *et al.* 2005) and India (Kumar *et al.* 2021, Kumar & Duggal 2019). Loquat has also been exploited in traditional medicine to cure kidney problems in Libya (El-Mokasabi *et al.* 2018), Ecuador (Tene *et al.* 2007), Mexico (Andrade-Cetto 2009). Additionally, it is used as an antidiabetic agent in Morocco (Chetoui *et al.* 2021, El Hachlafi *et al.* 2020, Hachi *et al.* 2016, Idm'hand *et al.* 2020, Khabbach *et al.* 2012, Merrouni *et al.* 2021, Merzouki *et al.* 2003, Zaouai *et al.* 2019, Ziyyat *et al.* 1997), Algeria (Nawel *et al.* 2019), Libya (El-Mokasabi *et al.* 2018), Portugal (Novais *et al.* 2004), Kenya (Odongo *et al.* 2018), Turkey (Kargiöglu & Ari 2017, Sargin 2015), Guatemala (Andrews *et al.* 2018), Ecuador (Bussmann 2002, Paniagua-Zambrana *et al.* 2020), Brazil (Trojan-Rodrigues *et al.* 2012) and China (Li *et al.* 2016). In addition, *E. japonica* is used to treat cardiovascular diseases in Morocco (Bellakhdar *et al.* 1991, Fakchich & Elachouri 2014, Merrouni *et al.* 2021), Limpopo (Maema *et al.* 2016), Cyprus (González-Tejero *et al.* 2008) and Portugal (Novais *et al.* 2004). Furthermore, it is used to treat the oral diseases in Mexico (Rosas-Piñón *et al.* 2012) and urinary disorders in Libya (El-Mokasabi *et al.* 2018), Ecuador (Tene *et al.* 2007) and Japan (Banno *et al.* 2005). In traditional Chinese medicine *E. japonica* is used as an anti-inflammatory (Banno *et al.* 2005, Li *et al.* 2016), anticancer (Li *et al.* 2016) and detoxifier (Hu *et al.* 2020). Loquat, is known by its traditional uses as an anti-emetic agent in Libya (El-Mokasabi *et al.* 2018), antiallergic in Morocco (Fakchich & Elachouri 2014, Merrouni *et al.* 2021), antihypercholesterolemic in Ecuador (Bussmann 2002, Tene *et al.* 2007) and Portugal (Novais *et al.* 2004), antiseptic in Pakistan (Azeem *et al.* 2020), a sedative in India (Kumar & Duggal 2019), an anti-infective in Libya (El-Mokasabi *et al.* 2018), Madagascar (Rabearivony *et al.* 2015) and in Limpopo (Semenya & Maroyi 2019).

In Ecuador the loquat is traditionally used against rheumatism (Tene *et al.* 2007). It is recommended as a tonic to treat headache in Algeria (Belhouala & Benarba 2021, Zatout *et al.* 2021) and to lower back pain in Italy (Menale *et al.* 2016). *E. japonica* is characterized by its many uses in traditional medicine, which differ from one country to another as they are represented in the table below (Table 2).

Other uses

In addition to its consumption as a fresh fruit, loquat is processed to develop a wide range of products such as juices, yogurts, jams, syrups, sauces, alcoholic beverages, jellies, chutneys, candied fruits and dried slices (Caballero & Fernández-Zamudio 2004, Dhiman *et al.* 2022, Ibrahim 2021, Li *et al.* 2016, Lim 2012, Small 2011, Soler *et al.* 2006, Sultan 2017, Tian *et al.* 2011). It is also used in fresh fruit salads, to prepare pies, tartlets and fillings (Lim 2012, Small 2011). The flowers are used as nectar for bees (Caballero & Fernández-Zamudio 2004, Li *et al.* 2016). Spiced fruits are also prepared with cinnamon, lemon, vinegar and cloves. The roasted seeds are eaten as a coffee substitute and the fresh roots as a cooked food (Lim 2012). The other parts of the plant (peel, leaves and seeds) are also used to prepare fermented tea (Soler *et al.* 2006, Tian *et al.* 2011), biscuits, noodles, tofu, starch, biodegradable film and as antioxidant to preserve oils (Dhiman *et al.* 2022). The tender branches are used as fodder and the old wood as firewood (Sultan 2017).

The processing of loquat provides opportunities to develop a wide variety of products, which can easily be transported to consumers around the world. The technologies used to extend its shelf life can three-fold increase its economic and market value as compared to its marketing as fresh fruit (Dhiman *et al.* 2022, Li *et al.* 2016, Sultan 2017, Tian *et al.* 2011).

Phytochemistry of *E. japonica*

A number of bioactive phytochemical compounds have been identified in the different parts of the *E. japonica* plant (Fig. 3). The analytical methods used are colorimetric assays, high performance liquid chromatography system with diode array detector (HPLC-DAD), high performance liquid chromatography coupled with electrospray ionization mass spectrometry (HPLC-ESI-MS), high-performance ion-exchange chromatography (HPIC), ultra-high performance liquid chromatography with diode array detector (UHPLC-DAD), ultra-performance liquid chromatography quadrupole-time-of-flight mass spectrometry (UPLC-Q-TOF-MS), nuclear magnetic resonance-mass spectrometry (NMR-MS) and high-resolution electrospray ionization mass spectrometry (HR-ESI-MS spectrum). So far 194 phytochemical compounds have been identified in different parts of loquat, which have been divided into triterpenes, sesquiterpene glycosides, flavonoids, phenolic acids, organic acids, lignans and megastigmane glycosides. Out of these bioactive components triterpenes and flavonoids are of major pharmacological significance (Kurnaz *et al.* 2024, Li *et al.* 2020a, Parrado Muñoz *et al.* 2024).

Mogole *et al.* (2020) carried out a qualitative and quantitative study on the phytochemical components of loquat leaves extracts. The results showed that the acetone extract was characterized by the presence of phenols, flavonoids, tannins, saponins, alkaloids, proteins, carbohydrates, glycosides and steroids. However, no saponins were found in the methanolic extract. Ethyl acetate and hexane extracts were characterized by the absence of alkaloids and saponins. The quantitative

analysis demonstrated that all the extracts contained phenolic and flavonoid compounds. The highest contents of phenolic compounds (3.810 ± 0.0036 mg GAE/g) and flavonoids (0.3833 ± 0.0016 mg QE/g) were observed in the methanolic extract. These results are similar to those reported by Gopal *et al.* (2019), who also showed the absence of saponins in the methanolic extract of leaves *E. japonica*.

The study performed by Khouya *et al.* (2022) showed that the aqueous extract of loquat leaves showed the polyphenol and flavonoid contents of 240.65 ± 12.56 mg of caffeic acid equivalents per g of the dry extract and 95.53 ± 9.04 mg of rutin equivalents per g of the dry extract, respectively. These contents were lower than that of thyme aqueous extract used as a reference. This extract was also characterized by the presence of 10 phenolic compounds including naringenin (10.93 ± 0.19 mg/g), procyanidin C1 (9.33 ± 0.16 mg/g), epicatechin (8.43 ± 0.04 mg/g) and rutin (7.55 ± 0.12 mg/g) as the main compounds. Fresh loquat leaves are rich in fiber (63.80%), carbohydrates (71.60%), low in sugars (0.80%), lipids (1.00%) and energy (205.00 Kcal/100 g). Potassium, magnesium and calcium are the main minerals present in the leaves with the values 953.80, 279.60 and 267.50 mg/100 g, respectively. The leaves also contained high amounts of vitamins B6, B2 and B12 as compared to the other vitamins. Bisso *et al.* (2022) reported that the hexane, ethyl acetate, chloroform and methanol extracts of loquat seeds, leaves and barks contained phenols, polyphenols, flavonoids and triterpenes, while the alkaloids were only present in the ethyl acetate extract from leaves and hexane extract from barks. Saponins were detected in methanol extracts of leaves and barks. The methanol extract of seeds and the hexane extract of leaves contained high amounts of phenolic compounds (270.07 mg GAE/g and 191.98 mg GAE/g, respectively) and flavonoids (34.62 mg QE/g and 38.03 mg QE/g, respectively).

The phytochemical analysis carried out by Pande and Akoh (2010) showed that the total contents of carotenoids in the whole fruit, peel and pulp is equal to 2.8 mg/100 g FW, 1.8 mg/100 g FW and 1.2 mg/100 g FW, respectively. While the polyphenol contents of the hydrophilic fractions of seeds, pulps, peels, whole fruits and leaves were higher in comparison to the lipophilic fractions. Total lipids are high in seeds ($18.5 \pm 2.1\%$) compared to fruits ($0.3 \pm 0.1\%$). Loquat fruit is characterized by the presence of alkaloids, triterpenes, flavonoids, carbohydrates and coumarins, while tannins and saponins were not detected (Abdel Raoof *et al.* 2021).

Rashed and Butnariu (2014) used the standard methods to determine the phytochemical contents in the methanolic extract of the loquat stem. They reported that this extract is characterized by the presence of carbohydrates, flavonoids, tannins, triterpenes and a low content of polyphenols.

Based on the results of these phytochemical studies, it can be concluded that the leaves, seeds, bark, fruits, and stems of *E. japonica* are characterized by the presence of phenols, polyphenols, flavonoids, and triterpenes, except for a low polyphenol content in the stems. Moreover, saponins are present in the leaves and bark of the loquat. The leaves and fruits are characterized by the presence of alkaloids and glucosides, with the latter also present in the stems. Tannins are present in the leaves and stems. Additionally, the leaves also contain proteins, carbohydrates, and steroids, while the fruits also embody carotenoids and coumarins.

Triterpenes

Various phytochemical studies conducted on different parts of *E. japonica* have isolated and identified 51 triterpenes to date. These triterpenes have been classified into three types, oleanane (19 types), ursane (39 types) and lupane (2 types) (Banno *et al.* 2005, De Tommasi *et al.* 1991, De Tommasi *et al.* 1992b, Dhiman *et al.* 2022, Ho *et al.* 2008, Huang *et al.* 2006, Ibrahim 2021, Jianhua *et al.* 2003, Jung *et al.* 1999, Li *et al.* 2009, Liang *et al.* 1990, Rashed & Butnariu 2014, Rollinger *et al.* 2010, Shimizu *et al.* 1986, Sultan 2017, Tan *et al.* 2015, Taniguchi *et al.* 2002, Uto *et al.* 2013, Wei *et al.* 2019, Zhou *et al.* 2007, Zhou *et al.* 2019). *E. japonica* is characterized by the presence of four major triterpenoid acids, which are ursolic acid, corosolic acid, oleanolic acid and maslinic acid (Dhiman *et al.* 2022, Li *et al.* 2020a, Taniguchi *et al.* 2002, Uto *et al.* 2017).

Sesquiterpene glycosides

The loquat leaves are characterized by the presence of twelve sesquiterpene glycosides (Ao *et al.* 2015, Chen *et al.* 2008, De Tommasi *et al.* 1990, De Tommasi *et al.* 1992a, Gai *et al.* 2022, Lee *et al.* 2004, Li *et al.* 2020b, Liu *et al.* 2016, Wu *et al.* 2021, Yanagisawa *et al.* 1988, Zhao *et al.* 2015). Because of their biological activities, they are considered as the potential bioactive compounds. Nerolidol-3-O- α -L-rhamnopyranosyl-(1-4)- α -L-rhamnopyranosyl-(1-2)-[α -L-rhamnopyranosyl-(1-6)]- β -D-glucopyranoside, nerolidol 3-O- α -L-rhamnopyranosyl-(1-4)- α -L-rhamnopyranosyl-(1-2)- β -D-glucopyranoside, nerolidol 3-O- α -L-rhamnopyranosyl-(1-2)-[α -L-rhamnopyranosyl-(1-6)]- β -D-glucopyranoside and nerolidol-3-O- α -L-arabinopyranosyl-(1-4)- α -L-rhamnopyranosyl-(1-2)-[α -L-rhamnopyranosyl-(1-6)]- β -D-glucopyranoside isolated from the leaves of *E. japonica* possess antidiabetic activities (Chen *et al.* 2008, Li *et al.* 2020b).

Table 2. Ethnomedicinal uses of *E. japonica*.

Country	Common name	Plant part used	Mode of preparation	Traditional uses	References
Morocco	Mzah, l-mzah, loquat of Japan, lamzah, ramzah, m'zaah	Leaves, fruits	Decoction, infusion, juice and crude extract	As an antidiarrheal agent for children, to treat digestive disorders, hypertension, diabetes, gout, allergy and cold	(Bellakhdar <i>et al.</i> 1991, Ben Akka <i>et al.</i> 2019, Chetoui <i>et al.</i> 2021, El Hachlafi <i>et al.</i> 2020, Fakchich & Elachouri 2014, Hachi <i>et al.</i> 2016, Idm'hand <i>et al.</i> 2020, Khabbach <i>et al.</i> 2012, Merrouni <i>et al.</i> 2021, Merzouki <i>et al.</i> 2000, Merzouki <i>et al.</i> 2003, Zaouai <i>et al.</i> 2019, Ziyat <i>et al.</i> 1997)
Algeria	Alnifalat, albashmalat, lmzah, hamzala	Leaves	Decoction, infusion	Headache, diabetes and body pain	(Belhouala & Benarba 2021, Nawel <i>et al.</i> 2019, Zatout <i>et al.</i> 2021)
Libya	Nasboli	Not specified	Not specified	Cough, renal stones, urinary tract infection, emetic, diabetes, ureterostenosis and renal colic	(El-Mokasabi <i>et al.</i> 2018)
Limpopo	Mohlatswa	Leaves	Decoction	Hypertension and tuberculosis	(Maema <i>et al.</i> 2016, Semenya & Maroyi 2019)
Madagascar	Pibasy	Leaves, stems	Decoction	Cough, infections during pregnancy and bilharzia	(Paniagua-Zambrana <i>et al.</i> 2020, Rabearivony <i>et al.</i> 2015)
Kenya	Lqogat	Fruits, barks	Chewed, boiled	Cough, asthma, chronic bronchitis, phlegm, high fever and gastro-enteric disorders	(Odongo <i>et al.</i> 2018)
Turkey	Yeni dünya, muşmul, muşmula, musmala	Flowers, leaves	Decoction, infusion	Common cold, cough, expectorant, asthma, bronchitis, diabetes and immune system	(Akaydin <i>et al.</i> 2013, Gürdal & Öztürk 2022, Kargiöglu & Ari 2017, Sargin 2015)
Cyprus	Not specified	Not specified	Not specified	Cardiovascular diseases	(González-Tejero <i>et al.</i> 2008)
Portugal	Nespereira	Leaves	Infusion	Antihypercholesterolemic, hypoglycemic, antidiarrhoeic, and antihypertensive	(Novais <i>et al.</i> 2004)
Spain	Nespereira, níspero de Japón	Leaves	Decoction	Constipation	(Benítez <i>et al.</i> 2010)
Italy	Niespolo d'o giappone	Leaves	Fumigation of decoction with leaves of <i>Foeniculum vulgare</i> Mill., <i>Matricaria chamomilla</i> L.	Diarrhea, lumbago, respiratory diseases and throat infections	(Menale <i>et al.</i> 2016)
Guatemala	Níspero	Seeds	Tea	Antidiabetic	(Andrews <i>et al.</i> 2018)

Mexico	Níspero	Leaves	Infusion	Kidney problems, cough, dental caries and gum diseases	(Andrade-Cetto 2009, Rosas-Piñón <i>et al.</i> 2012)
Brazil	Ameixa-do-Japão, nêspereira-do-Japão	Roots barks	Tea	Antidiabetic	(Trojan-Rodrigues <i>et al.</i> 2012)
Ecuador	Nispero	Leaves, flowers	Infusion	Liver diseases, to reduce cholesterol, to treat diabetes, as antacid, diuretic, gastritis, influenza, prostate, pneumonia, rheumatism and kidney problems	(Bussmann 2002, Paniagua-Zambrana <i>et al.</i> 2020, Tene <i>et al.</i> 2007)
Pakistan	Locat	Leaves	Decoction	Treat cough and as mouth wash	(Azeem <i>et al.</i> 2020)
China	Pi pa ye pipa	Leaves, fruits	Decoction	Antitussive, anti-inflammatory, chronic bronchitis, cirrhosis, hemoptysis, clearing away heat, toxic materials, diabetes, cancer and lung disease	(Banno <i>et al.</i> 2005, Hu <i>et al.</i> 2020, Li <i>et al.</i> 2016, Lu <i>et al.</i> 2022, Xiong <i>et al.</i> 2020)
Japan	Biwa	Leaves	Not specified	Diuretic, digestive and antipyretic agent	(Banno <i>et al.</i> 2005)
India	Loquathh, lokat	Fruits, flowers, leaves	Decoction	Sedative, against diarrhea, expectorant, cough, cold, relieve vomiting and thirst	(Kumar <i>et al.</i> 2021, Kumar & Duggal 2019)

The compound 3-O- α -L-rhamnopyranosyl-(1-4)-(α -L-rhamnopyranosyl-(1-2)-[(α -L-(4-trans-feruloyl)-rhamnopyranosyl-(1-6)]- β -D-glucopyranosyl nerolidol extracted from loquat leaves has a potent tissue factor inhibitor (Lee *et al.* 2004). Total sesquiterpene glycosides contained in the leaves have been reported to possess significant antioxidant and hepatoprotective effects (Jian *et al.* 2017).

Flavonoids

Sixty different types of flavonoids have been reported to be present in various parts of the *E. japonica*. Kaempferol 3-O-beta-glucoside, quercetin, quercetin 3-O-alpha-rhamnoside and naringenin have been identified as the main bioactive compounds present in the stems of *E. japonica* (Rashed & Butnariu 2014). While kaempferol has been reported to be the main compound in seeds (Barbi *et al.* 2018). The dominant compounds in loquat leaves are naringenin, procyanidin C1, epicatechin and rutin (Khouya *et al.* 2022).

Phenolic acids

Several studies have shown that *E. japonica* is characterized by the presence of numerous phenolic acids (twenty-eight phenolic acids). Xu and colleagues reported that caffeic acid, 4-O-caffeoylquinic acid, neochlorogenic acid, chlorogenic acid, 4-hydroxybenzoic acid, protocatechuic acid, o-coumaric acid, ellagic acid and ferulic acid are the most abundantly present phenolic acids in ripe fruits of *E. japonica* (Xu *et al.* 2014).

Organic acids

The number of organic acids present in fruits, play an important role in the development of their flavour. Numerous phytochemical studies have been carried out to determine the chemical composition of the organic acids of the loquat plant grown in many countries. It has been confirmed that the loquat plant contains twenty different organic acids (Abdel Raoof *et al.* 2021, Ahumada *et al.* 2017, Amorós *et al.* 2004, Chen *et al.* 2009, De Almeida Lopes *et al.* 2018, Dhiman *et al.* 2022, Ding *et al.* 1998, Koba *et al.* 2007, Pande & Akoh 2010, Pareek *et al.* 2014, Shaw & Wilson 1981, Silva *et al.* 2020, Sortino *et al.* 2022, Toker 2013). The malic acid has been identified as the major organic acid in loquat (Li *et al.* 2016, Shaw & Wilson 1981, Toker 2013), which represents almost 90% of all the ripe fruit acids (Ding *et al.* 1998).

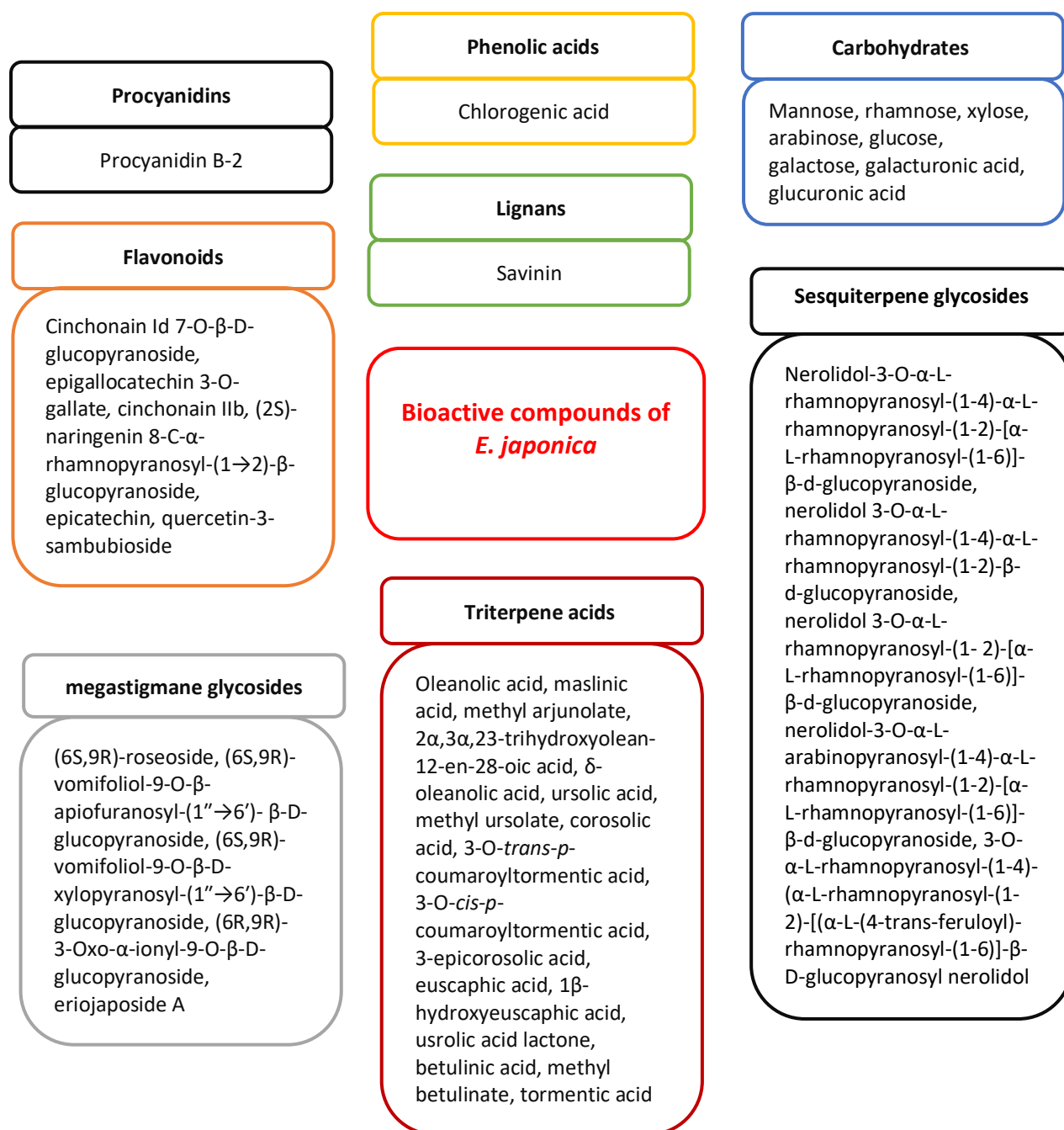
Lignans

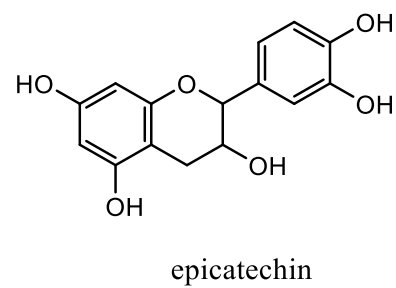
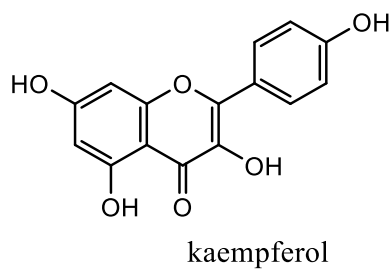
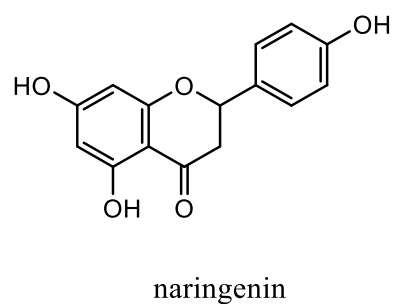
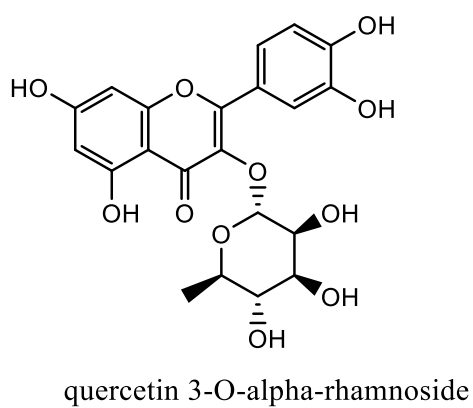
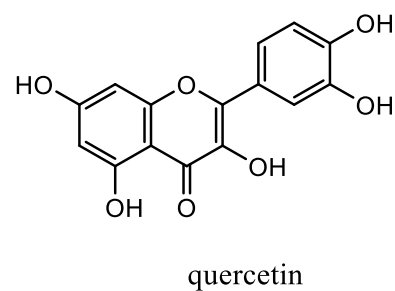
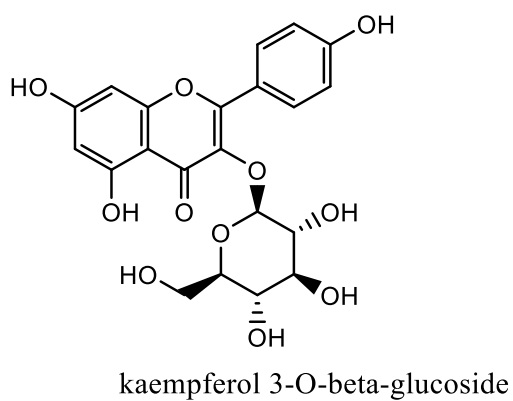
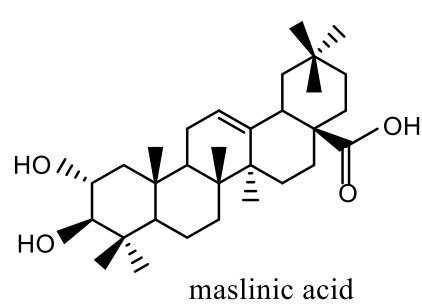
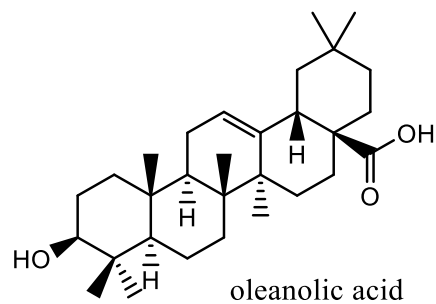
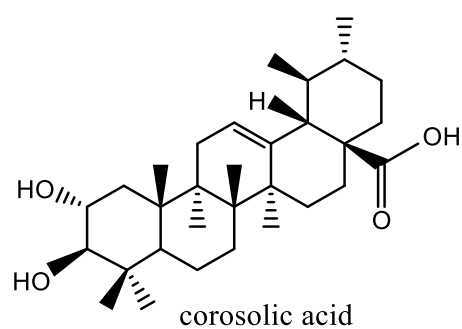
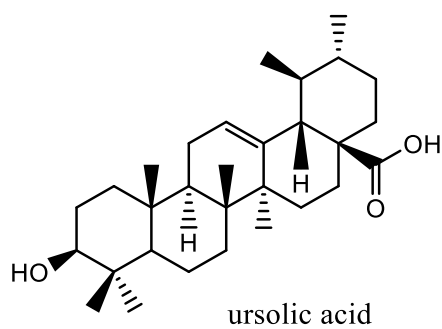
According to various phytochemical studies, *E. japonica* is characterized by the presence of ten different types of lignans in its leaves, roots and stems (Wu *et al.* 2003, Zhang *et al.* 2021a).

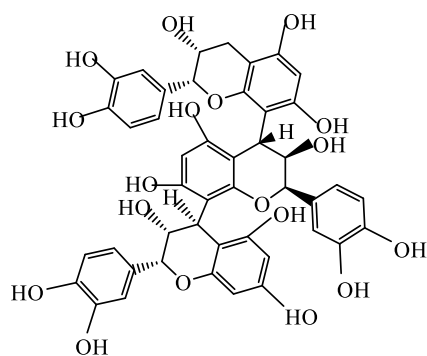
Megastigmane glycosides

Thirteen different megastigmane glycosides have been found to be present in various parts of *E. japonica* (Ito *et al.* 2002, Li *et al.* 2016, Wu *et al.* 2003). (6S,9R)-roseoside, (6S,9R)-vomifoliol-9-O- β -D-apiofuranosyl-(1" \rightarrow 6')- β -D-glucopyranoside, (6S,9R)-vomifoliol-9-O- β -D-xylopyranosyl-(1" \rightarrow 6')- β -D-glucopyranoside, (6R,9R)-3-Oxo- α -ionyl-9-O- β -D-glucopyranoside and eriojaposide A are the main megastigmane glycosides that have been isolated from loquat leaves. These have been shown to exhibit antitumor activities on mouse skin (Ito *et al.* 2002).

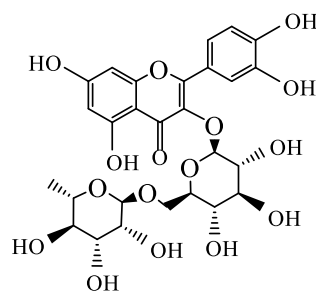
The chemical structures of the major compounds of *E. japonica* are shown in the following figure (Fig. 4). Each phenolic compound is present in one or several parts of the plant as illustrated in the following table (Table 3).

Figure 3. Bioactive compounds of *E. japonica*.

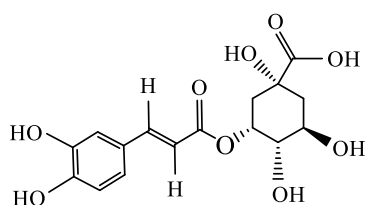




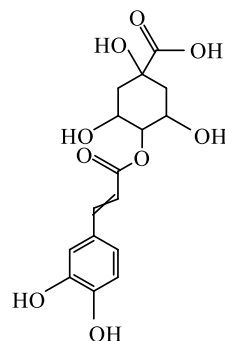
procyanidin C1



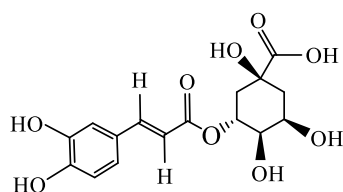
rutin



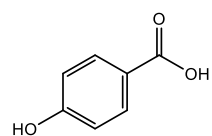
neochlorogenic acid



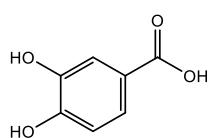
4-O-caffeoylquinic acid



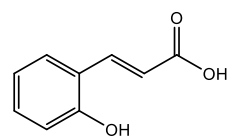
chlorogenic acid



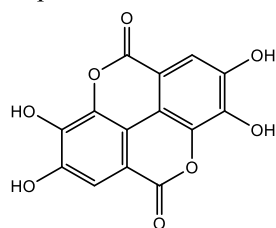
4-hydroxybenzoic acid



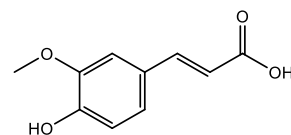
protocatechuic acid



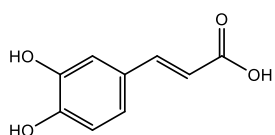
o-coumaric acid



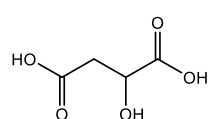
ellagic acid



ferulic acid



caffeic acid



malic acid

Figure 4. The chemical structure of the major compounds of *E. japonica* (drawn with ChemDraw Professional 15.0).

Table 3. List of phenolic compounds isolated from different parts of loquat.

Family	Compound name	Chemical formula	Part of the plant	Extraction method	References
Flavonoids	Quercetin	C ₁₅ H ₁₀ O ₇	Leaves, fruits, seeds, stems	Solvent extraction, infusion in distilled water, maceration	(Ibrahim 2021, Ito <i>et al.</i> 2000, Khouya <i>et al.</i> 2022), (Li <i>et al.</i> 2016), (Sultan 2017), (Ibrahim 2021, Rashed & Butnariu 2014)
	Quercetin-3-O-alpha-rhamnoside	C ₂₁ H ₂₀ O ₁₁		Ultrasound-assisted extraction combined with maceration, ultrasound-assisted extraction, solvent extraction, maceration	(Ferrerres <i>et al.</i> 2009, Liu <i>et al.</i> 2016), (Dhiman <i>et al.</i> 2022, Ferreres <i>et al.</i> 2009, Li <i>et al.</i> 2016, Sultan 2017, Zhang <i>et al.</i> 2015), (Jung <i>et al.</i> 1999), (Ibrahim 2021, Rashed & Butnariu 2014)
	Naringenin	C ₁₅ H ₁₂ O ₅		Infusion in distilled water, solvent extraction, extraction through decantation and filtration, maceration	(Khouya <i>et al.</i> 2022), (Abdel Raoof <i>et al.</i> 2021), (Barbi <i>et al.</i> 2018), (Ibrahim 2021, Rashed & Butnariu 2014)
	Quercetin-3-O-sambubioside	C ₂₆ H ₂₈ O ₁₆	Leaves, seeds, fruits	Ultrasound-assisted extraction combined with maceration, solvent extraction	(Ferrerres <i>et al.</i> 2009), (Jung <i>et al.</i> 1999), (Ferrerres <i>et al.</i> 2009, Li <i>et al.</i> 2016)
	Kaempferol-3-O-rhamnoside (Afzelin)	C ₂₁ H ₂₀ O ₁₀		Ultrasound-assisted extraction combined with maceration, infusion in distilled water, shaking and ultrasound, solvent extraction, ultrasound-assisted extraction	(Ferrerres <i>et al.</i> 2009, Khouya <i>et al.</i> 2022, Silva <i>et al.</i> 2020), (Jung <i>et al.</i> 1999), (Dhiman <i>et al.</i> 2022, Ferreres <i>et al.</i> 2009, Li <i>et al.</i> 2016, Sultan 2017, Zhang <i>et al.</i> 2015)
	Kaempferol 3-O-α-L-(2'',4''-di-E-feruloyl)-rhamnoside (feruloyl afzelin)	C ₄₁ H ₃₆ O ₁₆		Solvent extraction	(Kawahara <i>et al.</i> 2002), (Li <i>et al.</i> 2016)
	Kaempferol 3-O-α-L-(2'',4''-di-E-p-coumaroyl)-rhamnoside	C ₃₉ H ₃₂ O ₁₄			
	Kaempferol 3-O-α-L-(2'',4''-di-Z-p-coumaroyl)-rhamnoside	C ₃₉ H ₃₂ O ₁₄			

Quercetin-3-O-neohesperidoside	C ₂₇ H ₃₀ O ₁₆	Leaves, fruits	Ultrasound-assisted extraction combined with maceration	(Ferrerres <i>et al.</i> 2009), (Ferrerres <i>et al.</i> 2009, Li <i>et al.</i> 2016)
Quercetin-3-O-galactoside (hyperoside)	C ₂₁ H ₂₀ O ₁₂		Ultrasound-assisted extraction combined with maceration, ultrasound-assisted extraction	(Ferrerres <i>et al.</i> 2009, Liu <i>et al.</i> 2016), (Dhiman <i>et al.</i> 2022, Ferrerres <i>et al.</i> 2009, Li <i>et al.</i> 2016, Sultan 2017, Zhang <i>et al.</i> 2015)
Quercetin-3-O-glucoside (isoquercitrin)	C ₂₁ H ₂₀ O ₁₂		Ultrasound-assisted extraction combined with maceration, solvent extraction, shaking and ultrasound, ultrasound-assisted extraction	(Ferrerres <i>et al.</i> 2009, Ito <i>et al.</i> 2000, Liu <i>et al.</i> 2016, Silva <i>et al.</i> 2020, Wu <i>et al.</i> 2003), (Dhiman <i>et al.</i> 2022, Li <i>et al.</i> 2016, Sultan 2017, Zhang <i>et al.</i> 2015)
Quercetin-3-O-galactosyl-(1-6)-glucoside	C ₂₇ H ₃₀ O ₁₇			(Liu <i>et al.</i> 2016), (Li <i>et al.</i> 2016)
Quercetin-3-O-sophoroside	C ₂₇ H ₃₀ O ₁₇		Solvent extraction	(Ito <i>et al.</i> 2000, Liu <i>et al.</i> 2016), (Li <i>et al.</i> 2016)
Kaempferol-3-O-sophoroside	C ₂₇ H ₃₀ O ₁₆			
Kaempferol-3-O-neohesperidoside	C ₂₇ H ₃₀ O ₁₅		Ultrasound-assisted extraction combined with maceration	(Ferrerres <i>et al.</i> 2009), (Ferrerres <i>et al.</i> 2009, Li <i>et al.</i> 2016)
Kaempferol-3-O-sambubioside	C ₂₆ H ₂₈ O ₁₅		Solvent extraction	(Ito <i>et al.</i> 2000), (Li <i>et al.</i> 2016)
Kaempferol 3-O- α -rhamnopyranosyl-(1 \rightarrow 2)- β -D-glucopyranoside	C ₂₇ H ₃₀ O ₁₅		Solvent extraction, infusion in distilled water	(Ibrahim 2021, Ito <i>et al.</i> 2000, Khouya <i>et al.</i> 2022), (Ding <i>et al.</i> 2001, Li <i>et al.</i> 2016, Sultan 2017)
Epicatechin	C ₁₅ H ₁₄ O ₆		Infusion in distilled water	(Ito <i>et al.</i> 2002, Khouya <i>et al.</i> 2022), (Li <i>et al.</i> 2016)
Epigallocatechin gallate	C ₂₂ H ₁₈ O ₁₁		Shaking and ultrasound	(Liu <i>et al.</i> 2016, Silva <i>et al.</i> 2020), (Li <i>et al.</i> 2016)
Kaempferol-3-O-rutinoside	C ₂₇ H ₃₀ O ₁₅			
Kaempferol	C ₁₅ H ₁₀ O ₆	Leaves, seeds	Infusion in distilled water, extraction through decantation and filtration	(Khouya <i>et al.</i> 2022), (Barbi <i>et al.</i> 2018)

Kaempferol-3-O-beta-glucoside	C ₂₁ H ₂₀ O ₁₁	Leaves, fruits, stems	Shaking and ultrasound, ultrasound-assisted extraction, maceration	(Liu <i>et al.</i> 2016, Silva <i>et al.</i> 2020), (Li <i>et al.</i> 2016, Sultan 2017, Zhang <i>et al.</i> 2015), (Ibrahim 2021, Rashed & Butnariu 2014)
Quercetin-3-O-rutinoside (rutin)	C ₂₇ H ₃₀ O ₁₆	Leaves, seeds, fruits, flowers	Infusion in distilled water, shaking and ultrasound, extraction through decantation and filtration, solvent extraction	(Khouya <i>et al.</i> 2022, Liu <i>et al.</i> 2016, Silva <i>et al.</i> 2020), (Barbi <i>et al.</i> 2018), (Li <i>et al.</i> 2016), (Ahumada <i>et al.</i> 2017)
Kaempferol-3-O-galactoside	C ₂₁ H ₂₀ O ₁₁	Fruits	Ultrasound-assisted extraction	(Zhang <i>et al.</i> 2015)
Quercetin-7-α-L-rhamnoside	C ₂₁ H ₂₀ O ₁₁	Leaves	Solvent extraction	(Wu <i>et al.</i> 2003)
Kaempferol-xylose	C ₂₀ H ₁₈ O ₁₀		Shaking and ultrasound	(Silva <i>et al.</i> 2020)
Kaempferol-hexose malic acid	C ₂₅ H ₂₄ O ₁₅			
Naringenin hexoside	C ₂₁ H ₂₂ O ₁₀			
Naringenin-C-α-rhamnose-glucose	C ₂₇ H ₃₂ O ₁₄			
3-O-Methylquercetin	C ₁₆ H ₁₂ O ₇			
Malvidin-3-glucoside	C ₂₃ H ₂₅ O ₁₂ ⁺			
6,8-Di-C-β-glucopyranosylchrysin	C ₂₇ H ₃₂ O ₁₄			
O,C-rhamnosyl-glucosyl-luteolin	C ₂₇ H ₃₀ O ₁₅			
Lucenin-2 (6,8-di-C-β-glucopyranosyl luteolin)	C ₂₇ H ₃₀ O ₁₆			
Tricin di-O,O-hexoside	C ₂₉ H ₃₄ O ₁₇			
3-Hydro xylicariin-O-glucose rhamnose	C ₃₃ H ₄₀ O ₁₆			
Tetra-O-galloyl-hexoside I	C ₃₄ H ₂₈ O ₂₂			
Feruloyl glycoside	C ₁₆ H ₂₀ O ₉			
Taxifolin hexoside	C ₂₁ H ₂₂ O ₁₂			
Naringenin-6-C-(2''-O-acetyl)-glucoside	C ₂₃ H ₂₄ O ₁₁			
Naringenin-6-C-(2'',4'',6''-O-triacetyl)-glucoside	C ₂₇ H ₂₈ O ₁₃			
			Solvent extraction	(Park <i>et al.</i> 2019)

	Naringenin-6,8-di-C-glucoside	C ₂₇ H ₃₂ O ₁₅		Ultrasound-assisted extraction combined with maceration	(Ferrerres <i>et al.</i> 2009)
	(2S)-Naringenin 8-C- α -rhamnopyranosyl – (1→2)- β -glucopyranoside	C ₂₆ H ₃₀ O ₁₅		Solvent extraction	(Ito <i>et al.</i> 2000, Ito <i>et al.</i> 2002)
	Cinchonain Id 7-O- β -D-glucopyranoside	C ₃₀ H ₃₀ O ₁₄			
	Procyanidin oligomer				
	(2R)-Naringenin 8-C- α -rhamnopyranosyl – (1→2)- β -glucopyranoside	C ₂₆ H ₃₀ O ₁₅			(Ito <i>et al.</i> 2000)
	Cinchonain Ia	C ₂₄ H ₂₀ O ₉			
	Gallocatechin	C ₁₅ H ₁₄ O ₇			(Tao <i>et al.</i> 2022)
	Gallocatechingallate	C ₂₂ H ₁₈ O ₁₁			
	Afzelechin	C ₁₅ H ₁₄ O ₅			
	Procyanidin B-2	C ₃₀ H ₂₆ O ₁₂		Solvent extraction, shaking and ultrasound	(Ito <i>et al.</i> 2000, Ito <i>et al.</i> 2002, Silva <i>et al.</i> 2020)
	Procyanidin C-1	C ₄₅ H ₃₈ O ₁₈		Solvent extraction, infusion in distilled water	(Ito <i>et al.</i> 2000, Ito <i>et al.</i> 2002, Khouya <i>et al.</i> 2022)
	Isorhamnetin 3-O-glucoside	C ₂₂ H ₂₂ O ₁₂		Soxhlet solvent extraction	(Louati <i>et al.</i> 2003)
	Isorhamnetin 3-O-galactoside	C ₂₂ H ₂₂ O ₁₂			
	C- schaftoside glycoside				
	Cinchonain IIb	C ₃₉ H ₃₂ O ₁₅	Leaves, bark of the stems		(Ito <i>et al.</i> 2002), (Ibrahim 2021)
	Catechin	C ₁₅ H ₁₄ O ₆	Bark of the stems, fruits, leaves, seeds	Solvent extraction, shaking and ultrasound, solvent extraction	(Ibrahim 2021), (Abdel Raoof <i>et al.</i> 2021), (Ibrahim 2021, Silva <i>et al.</i> 2020, Tao <i>et al.</i> 2022), (Sultan 2017)
Phenolic acids	Ellagic acid	C ₁₄ H ₆ O ₈	Fruits, leaves	Solvent extraction, shaking and ultrasound	(Abdel Raoof <i>et al.</i> 2021, Ibrahim 2021, Sultan 2017, Xu <i>et al.</i> 2014), (Ibrahim 2021, Silva <i>et al.</i> 2020)
	3,4,5-trihydroxybenzoic acid (gallic acid)	C ₇ H ₆ O ₅		Solvent extraction	(Abdel Raoof <i>et al.</i> 2021, Li <i>et al.</i> 2016), (Ibrahim 2021)
	3-Caffeoylquinic acid (neochlorogenic acid)	C ₁₆ H ₁₈ O ₉		Ultrasound-assisted extraction combined with	(Dhiman <i>et al.</i> 2022, Ding <i>et al.</i> 2001, Ferreres <i>et al.</i> 2009, Ibrahim 2021, Li <i>et al.</i>

			maceration, solvent extraction, ultrasound-assisted extraction	2016, Sultan 2017, Xu <i>et al.</i> 2014, Zhang <i>et al.</i> 2015), (Ferrerres <i>et al.</i> 2009, Ito <i>et al.</i> 2000)
4-O-caffeoylquinic acid (cryptochlorogenic acid)	C ₁₆ H ₁₈ O ₉		Solvent extraction, ultrasound-assisted extraction	(Dhiman <i>et al.</i> 2022, Ding <i>et al.</i> 2001, Ibrahim 2021, Li <i>et al.</i> 2016, Sultan 2017, Xu <i>et al.</i> 2014, Zhang <i>et al.</i> 2015), (Ito <i>et al.</i> 2000)
3-p-Coumaroylquinic acid	C ₁₆ H ₁₈ O ₈		Ultrasound-assisted extraction combined with maceration, shaking and ultrasound	(Dhiman <i>et al.</i> 2022, Ferrerres <i>et al.</i> 2009, Li <i>et al.</i> 2016), (Ferrerres <i>et al.</i> 2009, Silva <i>et al.</i> 2020)
4-O-p-Coumaroylquinic acid	C ₁₆ H ₁₈ O ₈		Ultrasound-assisted extraction combined with maceration, solvent extraction	(Li <i>et al.</i> 2016), (Ferrerres <i>et al.</i> 2009, Ito <i>et al.</i> 2000)
5-p-Coumaroylquinic acid	C ₁₆ H ₁₈ O ₈		Ultrasound-assisted extraction combined with maceration, ultrasonic-assisted extraction, shaking and ultrasound	(Ferrerres <i>et al.</i> 2009, Li <i>et al.</i> 2016, Zhang <i>et al.</i> 2021a), (Ferrerres <i>et al.</i> 2009, Silva <i>et al.</i> 2020)
4-Feruloylquinic acid	C ₁₇ H ₂₀ O ₉		Ultrasound-assisted extraction combined with maceration	(Li <i>et al.</i> 2016), (Ferrerres <i>et al.</i> 2009)
5-Feruloylquinic acid	C ₁₇ H ₂₀ O ₉		Ultrasound-assisted extraction combined with maceration, ultrasound-assisted extraction, shaking and ultrasound	(Dhiman <i>et al.</i> 2022, Ding <i>et al.</i> 2001, Ferrerres <i>et al.</i> 2009, Ibrahim 2021, Li <i>et al.</i> 2016, Sultan 2017, Zhang <i>et al.</i> 2015), (Ferrerres <i>et al.</i> 2009, Silva <i>et al.</i> 2020)
4-O-β-glucopyranosyl-cis-p-coumaric acid	C ₁₅ H ₁₈ O ₈	Leaves, flowers	Solvent extraction	(Ito <i>et al.</i> 2000), (Ahumada <i>et al.</i> 2017)
trans-cinnamic acid	C ₉ H ₈ O ₂	Seeds	Extraction through decantation and filtration	(Barbi <i>et al.</i> 2018)
Benzoic acid	C ₇ H ₆ O ₂		Extraction under reflux	(Jeong <i>et al.</i> 2014)
3,4-dihydroxybenzoic acid (protocatechuic acid)	C ₇ H ₆ O ₄	Fruits, leaves, seeds	Solvent extraction,	(Dhiman <i>et al.</i> 2022, Ding <i>et al.</i> 2001, Ibrahim 2021, Li <i>et al.</i> 2016, Sultan 2017, Xu <i>et al.</i> 2014), (Khouya <i>et al.</i> 2022), (Barbi <i>et al.</i> 2018)

			infusion in distilled water, extraction through decantation and filtration	
p-Coumaric acid	C ₉ H ₈ O ₃	Fruits	Extraction through decantation and filtration	(Ding <i>et al.</i> 2001, Li <i>et al.</i> 2016, Sultan 2017), (Ibrahim 2021), (Barbi <i>et al.</i> 2018)
4-Hydroxybenzoic acid	C ₇ H ₆ O ₃		Solvent extraction	(Ibrahim 2021, Xu <i>et al.</i> 2014)
Syringic acid	C ₉ H ₁₀ O ₅			(Abdel Raoof <i>et al.</i> 2021)
Methyl gallate	C ₈ H ₈ O ₅			(Li <i>et al.</i> 2016)
2-Hydroxybenzoic acid	C ₇ H ₆ O ₃			(Dhiman <i>et al.</i> 2022, Ding <i>et al.</i> 2001, Sultan 2017)
Hydroxybenzoic acid	C ₇ H ₆ O ₃			
Sinapoyl glucoside	C ₁₇ H ₂₂ O ₁₀		Ultrasound-assisted extraction combined with maceration	(Ferrerres <i>et al.</i> 2009)
2-Hydroxycinnamic acid (o-coumaric acid)	C ₉ H ₈ O ₃		Solvent extraction	(Dhiman <i>et al.</i> 2022, Ding <i>et al.</i> 2001, Ibrahim 2021, Li <i>et al.</i> 2016, Sultan 2017, Xu <i>et al.</i> 2014)
4-Hydroxy-3-methoxycinnamic acid (ferulic acid)	C ₁₀ H ₁₀ O ₄			(Abdel Raoof <i>et al.</i> 2021, Dhiman <i>et al.</i> 2022, Ding <i>et al.</i> 2001, Ibrahim 2021, Li <i>et al.</i> 2016, Sultan 2017, Xu <i>et al.</i> 2014)
3,4-dihydroxycinnamic acid (caffeic acid)	C ₉ H ₈ O ₄	Fruits, flowers leaves, seeds	Solvent extraction, shaking and ultrasound, solvent extraction, extraction under reflux	(Abdel Raoof <i>et al.</i> 2021, Dhiman <i>et al.</i> 2022, Ibrahim 2021, Li <i>et al.</i> 2016, Sultan 2017, Xu <i>et al.</i> 2014), (Ahumada <i>et al.</i> 2017), (Ibrahim 2021, Silva <i>et al.</i> 2020), (Jeong <i>et al.</i> 2014)
5-Caffeoylquinic acid (chlorogenic acid)	C ₁₆ H ₁₈ O ₉		Solvent extraction, ultrasound-assisted extraction, ultrasound-assisted extraction combined with maceration, infusion in distilled water, shaking and ultrasound, extraction through decantation and	(Abdel Raoof <i>et al.</i> 2021, Dhiman <i>et al.</i> 2022, Ding <i>et al.</i> 2001, Ferrerres <i>et al.</i> 2009, Ibrahim 2021, Li <i>et al.</i> 2016, Xu <i>et al.</i> 2014, Zhang <i>et al.</i> 2015), (Ahumada <i>et al.</i> 2017), (Ferrerres <i>et al.</i> 2009, Ito <i>et al.</i> 2000, Khouya <i>et al.</i> 2022, Silva <i>et al.</i> 2020), (Barbi <i>et al.</i> 2018, Jeong <i>et al.</i> 2014, Jung <i>et al.</i> 1999)

			filtration, extraction under reflux	
Lignans	1-O-feruloyl- β -D-glucopyranose	C ₁₆ H ₂₀ O ₉	Leaves	Solvent extraction (Ito <i>et al.</i> 2000)
	Digalloyl-hexoyl-ellagic acid	C ₃₅ H ₂₆ O ₂₀		Shaking and ultrasound (Silva <i>et al.</i> 2020)
	Caffeoylquinic acid	C ₁₆ H ₁₈ O ₉		
	Dimethylmatairesinol	C ₂₂ H ₂₆ O ₆	Leaves, roots, stems	Ultrasonic-assisted extraction (Zhang <i>et al.</i> 2021a)
	Sesamin	C ₂₀ H ₁₈ O ₆		
	Lariciresinol	C ₂₀ H ₂₄ O ₆		
	Secoisolariciresinol	C ₂₀ H ₂₆ O ₆		
	Liguersinol 9'-O- β -D-xylopyranoside	C ₂₇ H ₃₆ O ₁₂	Leaves	Solvent extraction (Wu <i>et al.</i> 2003)
	Eriobitrin	C ₂₁ H ₂₆ O ₁₀		
	Liguersinol	C ₂₂ H ₂₈ O ₈		
	Isoeriobitrin	C ₂₁ H ₂₆ O ₁₀		
	2,6-dimethoxy-4-(2-propenyl) phenol	C ₁₁ H ₁₄ O ₃		
2,6-dimethoxy-4-(2-propenyl) phenol 1-O- β -D-glucopyranoside				

Biological activities of *E. japonica*

Ethnomedicinal uses serve as a key reference for evaluating the pharmacological activities. Scientific data has identified a significant correlation between traditional practices and modern pharmacological effects. The pharmacological activities attributed to *E. japonica* are depicted in Fig. 5, showing its therapeutic potential.

Antioxidant activity

The antioxidant activity of methanolic extracts from *E. japonica* leaves and its fractions was assessed through the free radical scavenging test of 1,1-diphenyl-2-picrylhydrazyl (DPPH), lipid peroxidation assay using mouse liver homogenates, and free radical generation test in hepatocytes via the dichlorofluorescein (DCF) method. The MeOH extract, along with the n-BuOH and EtOAc fractions, exhibited potent free radical scavenging activity (DPPH), with SC_{50} values (50% scavenging concentrations) of 9.25, 5.31, and 2.76 $\mu\text{g/mL}$, respectively. This difference indicates the higher efficacy of the polar fractions, which contain bioactive metabolites with stronger antioxidant properties. Notably, two compounds isolated from the n-BuOH fraction, chlorogenic acid and quercetin-3-sambubioside, demonstrated significant antioxidant potential, with SC_{50} values of 6.35 and 9.62 μM , respectively, highlighting their potential as key contributors to the antioxidant mechanism. The lipid peroxidation assay using TBA indicated that the MeOH extract, as well as the EtOAc and n-BuOH fractions, effectively inhibited lipid peroxidation by 62%, 62%, and 68%, respectively. Whereas the CH_2Cl_2 fraction showed no inhibition, indicating the absence of bioactive compounds involved in the prevention of lipid oxidation. Regarding the hepatocyte free radical generation, the MeOH extract (0.5 mg/mL), and the fractions (0.2 mg/mL), alongside the compounds isolated from the n-BuOH and EtOAc fractions, demonstrated significant inhibitory activity. However, the CH_2Cl_2 fraction, 2 α -hydroxyursolic acid, and ursolic acid, did not exhibit antioxidant properties, indicating that the antioxidant potential is strongly influenced by the structural characteristics of the compounds involved (Jung *et al.* 1999). Furthermore, Pawłowska *et al.* (2023) reported that the ethanolic extract of *E. japonica* leaves demonstrated superior antioxidant and anticancer potential in comparison to the fruit extract. Analysis revealed that these extracts contained 25 distinct phenolic compounds, which exhibited a strong correlation with their antiproliferative properties.

Moreover, the antioxidant capacity of *E. japonica* flowers was evaluated using three different methods: 2,2'-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), ferric reducing antioxidant power (FRAP), and DPPH. The results demonstrated that the antioxidant capacity followed this ranking: ABTS > DPPH > FRAP. Among the tested solvents, the methanolic extract of the flowers showed the strongest antioxidant activity. The antioxidant effects varied among cultivars, with the highest activity was observed in Dayeyangdun, while Jiajiao displayed the lowest. The antioxidant activity of the flowers also fluctuated according to their developmental stage, following the order: stage 3 (fully open) > stage 2 (partially open) > stage 4 (fallen flower petals) > stage 1 (flower bud). The analysis of the antioxidant capacity of different floral tissues showed that the petals were richest in antioxidants, followed by pistil and stamens. These findings highlighted a strong correlation between antioxidant capacity and the concentration of flavonoids and phenolic compounds. Additionally, the ABTS test exhibited the strongest correlation with the levels of these bioactive metabolites (Zhou *et al.* 2011).

In a separate study, Barbi *et al.* (2018) investigated the antioxidant capacity of phenolic extracts from loquat seed starch (LSS), obtained from three urban reforestations (A, B, C) and commercial fruits (D), at two maturity stages: ripe (RI) and unripe (UNR). The tests used included DPPH, ABTS, and FRAP. The antioxidant activity measured by the DPPH test ranged from 24.87 to 240.94 μmol Trolox equivalent (TE)/100 g of starch sample. The ABTS test values varied between 49.82 and 258.27 μmol TE/100 g, while the FRAP test results fell within the range of 24.43 to 155.72 μmol TE/100 g. Across all three tests, unripe the starch samples (UNS) from the three reforestations exhibited greater antioxidant activity compared to ripe fruit. Among the analyzed samples, sample B (RI and UNR) displayed the highest antioxidant activity, whereas the commercial sample showed the lowest. This enhanced antioxidant activity is linked to the elevated concentration of phenolic compounds in these extracts, particularly due to the presence of kaempferol and 5-caffeoylquinic acid.

Finally, the antioxidant potential of seven loquat fruits cultivars from the Antalya region, Türkiye was determined using three different methods: DPPH, FRAP, and ABTS. Significant variations in antioxidant activity were observed among the cultivars. Among all three tests (DPPH, FRAP, and ABTS), cultivar 'Akko XIII' exhibited the highest antioxidant capacity, with values of 2.85, 3.11, and 1.84 μmol TE per g of sample, respectively. Conversely, the lowest antioxidant potential was recorded for cultivar 'KKTC-3' in the DPPH test (5.85 μmol TE/g), 'Guzelyurt 6' in the FRAP test (5.91 μmol TE/g), and 'Hafif Cukurgobek' in the ABTS test (4.53 μmol TE/g). These results correlate with the total phenolic content of loquat, reinforcing its strong antioxidant potential (Ercisli *et al.* 2012).

Overall, these research studies highlight the strong antioxidant potential of *E. japonica*, whose effectiveness however, varies according to the type of extract, cultivar, and developmental stage. This activity is mainly attributed to the flavonoids and phenolic compounds, reinforcing the interest of this plant for medicinal applications.

Antimicrobial activity

The antimicrobial effects of methanolic extract from loquat stems harvested in Egypt were evaluated by Rashed and Butnariu (2014) against various bacterial and fungal strains. The results showed significant inhibition of *Candida albicans* growth, with a minimum inhibitory concentration (MIC) of approximately 16 µg/mL, whereas no effect was observed on the other tested strains. These findings suggest that the methanolic extract of *E. japonica* stems exhibits selective antifungal activity against *Candida albicans* infections.

Additionally, Abdel Raoof *et al.* (2021) reported that the methanolic extract of *E. japonica* fruits exhibited significant antimicrobial activity against several bacteria, including *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, and *Salmonella typhimurium*, with MIC values of 100, 200, 200, and 200 mg/mL, respectively. However, the polysaccharides isolated from the fruits showed selective inhibition of *S. aureus* and *B. cereus*, with an MIC value of 500 mg/mL. Notably, none of the tested extracts exhibited any antifungal activity against *Candida albicans* and *Aspergillus brasiliensis*, suggesting that the active compounds primarily target bacteria rather than fungi.

In another study, Bae *et al.* (2005) investigated the effects of epicatechin isolated from loquat leaves against thirteen bacterial species. The results demonstrated a general inhibition of bacterial growth, with strong efficacy against *B. cereus*, *Listeria monocytogenes*, and *S. aureus*. Conversely, Zhou *et al.* (2019) reported that the ethanolic extract of *E. japonica* leaves was not toxic to the bacterial strains tested, showing MIC values ≥ 5 mg/mL, which may suggest lower antimicrobial activity compared to other studied extracts.

Bisso *et al.* (2022) evaluated the antifungal activity of *E. japonica* leaf, seed, and bark extracts, prepared using various solvents (hexane, chloroform, ethyl acetate, and methanol), against nine isolates of *Cryptococcus neoformans* using the broth microdilution method. Among these, the methanolic seed extract (MeS) and the hexane leaf extract (HeL) were the most active, with a MIC of 32 µg/mL and a minimum fungicidal concentration (MFC) of 128 µg/mL. The combination of these extracts with reference antifungals, such as nystatin and clotrimazole, significantly reduced MIC values, with reductions of up to 32-fold. The observed synergistic effect suggests that the flavonoids and phenolic compounds play a crucial role in the inhibition of pathogenic fungi.

Similarly, Shen *et al.* (2021) demonstrated that loquat leaf extract (LLE) exhibited significant antifungal activity against *Penicillium digitatum*, with a MIC of 0.625 mg/mL and an MFC of 1.25 mg/mL. The extract was found to inhibit the growth and germination of *P. digitatum* spores in a dose-dependent manner, leading to morphological alterations, increased membrane permeability, and disruptions in fungal energy metabolism. These effects suggest that its antifungal action is primarily driven by the disruption of cell membranes and impact on the essential metabolic pathways.

Ustaömer *et al.* (2020) investigated the antifungal effects of hot-water, methanolic, and ethanolic extracts, as well as the essential oil derived from loquat bark, sapwood, and heartwood. Their results indicated that the ethanolic extract and essential oils from the heartwood and bark, as well as the methanolic extract from the sapwood, completely inhibited the growth of *Coniophora puteana* after seven days of incubation. However, the antifungal effects of the methanolic extract from the heartwood and bark, along with the ethanolic extract and essential oil from the sapwood, decreased after only three days of incubation, suggesting an instability in the antimicrobial activity over time.

These studies highlight that the antimicrobial activity of *E. japonica* varies depending on the plant organ used (leaves, fruits, stems, seeds, wood), the type of extract (methanolic, ethanolic, hexane, aqueous), and the microbial target (bacteria or fungi). While certain extracts, such as those from stems and seeds, exhibit strong antifungal properties, others, like fruit extracts, are more effective against bacteria. This diversity of biological activities paves the way for further research on the use of loquat extracts in developing new natural antimicrobial agents, with their potential applications in medicine as well as in the food industry to combat bacterial and fungal infections.

Anti-inflammatory activity

The n-BuOH fraction of *E. japonica* leaves (LEJ) exhibits notable anti-inflammatory properties, as demonstrated in a murine peritoneal macrophage model using C57BL/6 mice stimulated with rIFN-γ/LPS. LEJ treatment significantly inhibited nitric

oxide (NO) production in a dose-dependent manner, reaching a maximum suppression of 87.7% at 500 µg/mL. This reduction was accompanied by a marked decrease in the expression of inducible NO synthase (iNOS) and cyclooxygenase-2 (COX-2), two enzymes that are critical in propagating the inflammatory responses. Consequently, LEJ also suppressed the secretion of key pro-inflammatory cytokines, tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6), indicating a broader regulatory effect on inflammatory signaling pathways. Further mechanistic analysis revealed that LEJ interferes with NF-κB nuclear translocation, a pivotal step in initiating the inflammatory gene expression. In macrophages, co-incubated with rIFN-γ/LPS plus LEJ, the NF-κB levels decreased in the nucleus while increasing in the cytosol, suggesting an inhibition of its activation. This attenuation of NF-κB activity underscores LEJ's role in modulating inflammation at a transcriptional level, potentially reducing the cellular response to inflammatory stimuli. These findings highlight the therapeutic potential of *E. japonica* leaf extracts in controlling inflammatory conditions (Cha *et al.* 2011).

In line with the previous findings, another study examined the anti-inflammatory potential of *E. japonica* leaf infusion extract (EJLE) in Swiss mice, evaluating its effects on both acute and persistent experimental joint inflammation. Various established models were employed, including carrageenan-induced acute pleural inflammation, carrageenan-induced paw edema, zymosan-induced acute knee inflammation, and Complete Freund's Adjuvant (CFA)-induced persistent inflammation. In the carrageenan-induced pleurisy model, EJLE significantly reduced leukocyte migration (25, 33, and 26%), protein extravasation into the intrapleural space (23, 25, and 25%), and NO production (39%, 45%, and 33%) at doses of 30, 100, and 300 mg/kg BW (body weight), respectively. Similarly, in the paw edema model, EJLE inhibited the edema formation by 75% compared to control group, while also demonstrating antihyperalgesic and anti-allodynic effects. In the zymosan-induced knee inflammation model, EJLE resulted in a $43 \pm 6\%$ reduction in leukocyte migration, a 68% decrease in edema formation and a complete suppression of hyperalgesia. Additionally, in the persistent inflammation model, oral administration of EJLE led to a $73 \pm 2\%$ inhibition of edema formation, a complete suppression of mechanical hyperalgesia, and a $50 \pm 8\%$ reduction in cold allodynia relative to the control group. These results underscore the strong anti-inflammatory potential of *E. japonica*, that is likely mediated through the suppression of key inflammatory mediators such as prostaglandin E₂ (PGE₂), COX-2, and NO. The observed effects appear to be driven by the downregulation of enzyme expression (iNOS, COX-2) and the inhibition of NF-κB activation, thereby limiting its nuclear translocation and dampening the inflammatory response. This anti-inflammatory effect may be attributed to the presence of acid triterpenes, such as corosolic acid, oleanolic acid, and ursolic acid, which have been identified in EJLE (Kuraoka-Oliveira *et al.* 2020).

In another study, the anti-inflammatory effects of 16 different triterpene acids isolated from *E. japonica* leaves were evaluated against 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced ear inflammation in mice. The results indicated that all triterpene acids inhibited the TPA-induced inflammation with an IC₅₀ ranging from 0.03 to 0.43 mg/ear. The weakest inhibition was observed with 3-O-trans-p-coumaroyltormentic acid. Methyl ursolate exhibited the strongest anti-inflammatory effects. These triterpene acids demonstrated similar or superior anti-inflammatory activities compared to the reference drugs such as indomethacin and hydrocortisone (Banno *et al.* 2005).

Overall, these findings confirm that the anti-inflammatory effects of *E. japonica* are primarily linked to the presence of acid triterpenes, including corosolic acid, oleanolic acid, and ursolic acid. These compounds play a crucial role in modulating the inflammatory responses by inhibiting NF-κB signaling and suppressing the production of pro-inflammatory mediators.

Antitumor activities

The anti-carcinogenic effects of triterpene acids isolated from *E. japonica* leaves were evaluated both in vitro and in vivo by Banno *et al.* (2005). The study examined the ability of these compounds to inhibit the activation of TPA-induced Epstein-Barr virus early antigen (EBV-EA) in Raji cells (human lymphoblastoid cells carrying the EBV genome; non-producing type). In-vivo, the two-step mouse skin carcinogenesis assay was performed using 7,12- dimethylbenz[α]anthracene (DMBA) initiation followed by TPA promotion. The in-vitro study revealed that all tested compounds inhibited the TPA-induced activation of EBV-EA. Among them, euscaphic acid (compound 12) and 1β-hydroxyeuscaphic acid (compound 13) demonstrated the strongest inhibitory effects, with IC₅₀s values of 306 and 291 mol ratio/32 pmol TPA, respectively. The group treated with euscaphic acid (12) exhibited a progressive decline in the percentage of mice carrying papillomas: 27% at 10 weeks, 53% at 15 weeks, and 73% at 18 weeks of tumor promotion, in contrast to the positive control group, where 100% of the mice developed papillomas within the first 10 weeks. This effect was further validated in a study by Ito *et al.* (2002), which evaluated the antitumor properties of procyanidins, megastigmane glycosides, and flavonoids isolated from *E. japonica* leaves using the same experimental models. Most compounds, except procyanidin C-1 and procyanidin oligomer, exhibited significant EBV-EA inhibition (60-80%) at a concentration of 500 M ratio/TPA. Among them, procyanidin B-2 and roseoside caused the highest inhibitory effects. In-vivo, procyanidin B-2 and roseoside delayed the carcinogenesis initiated by DMB or

peroxynitrite and promoted by TPA, further reinforcing their potential as anti-cancer agents. These results indicate that triterpenic acids, particularly euscaphic acid and 1 β -hydroxyeuscaphic acid, along with megastigmane glucosides such as roseoside and flavonoids like procyanidin B-2, extracted from the leaves of *E. japonica*, exhibit potent anticancer activities. This effect is primarily attributed to their ability to inhibit both the initiation and proliferation of tumor cells.

On the other hand, another study was performed to determine the cytotoxic and apoptotic effects of the polysaccharide EJP90-1, extracted from loquat leaves, and its selenylation-modified form, EJP90-1-Se, on tumor cells (HepG2 and A549) using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. The effects of EJP90-1-Se on tumors and angiogenesis were also evaluated in-vivo using the zebrafish xenograft model. The in-vitro study showed that EJP90-1 and EJP90-1-Se inhibited tumor cell proliferation, with maximum inhibition rates of 20.1% and 83.7% of HepG2, respectively, and 21.3% and 66.5% of A549 respectively. The results indicated that selenylation enhanced the effects of EJP90-1, and that EJP90-1-Se suppressed the HepG2 cell proliferation more effectively than A549 cells. The in-vivo study revealed that EJP90-1-Se inhibited the growth, proliferation and migration, and angiogenesis of HepG2 cell in a dose-dependent manner. Therefore, polysaccharides extracted from loquat leaves demonstrate significant anticancer activity by inhibiting tumor cell growth, proliferation, migration, and angiogenesis. Furthermore, selenylation enhances these effects, reinforcing their therapeutic potential (Zhang *et al.* 2021b).

Hsieh *et al.* (2021) evaluated the anticancer activity of cell suspension culture extracts from *E. japonica* (EJCE) against prostate cancer (PCa). The results demonstrated that EJCE inhibited the expression of sterol regulatory element-binding protein-1 (SREBP-1) and fatty acid synthase (FASN). Furthermore, it reduced the intracellular fatty acid levels, lipid droplet accumulation, androgen receptors (ARs), and prostate-specific antigen (PSA). EJCE suppressed tumor growth and induced tumor cell apoptosis in xenograft mouse models, highlighting its potential as a powerful anti-PCa agent.

These studies have revealed that various chemical compounds, such as triterpenes, flavonoids, megastigmane glucosides, and polysaccharides extracted from *E. japonica* leaves, exhibit remarkable anticancer properties.

Antidiabetic effects

Khouya *et al.* (2022) evaluated the dose dependent (150, 200 and 250 mg/kg BW/day) antidiabetic and hypolipidemic effects of the aqueous extracts from the leaves of *E. japonica* (LLE), collected from the Beni Snassen Mountains in Morocco, using a rat model fed a high-fat and glucose (HFG) diet. The effects were compared with two reference antidiabetics: pravastatin (20 mg/kg BW/day) and metformin (50 mg/kg BW/day). LLE reduced the plasma glucose and insulin levels, decreased oxidative stress and hyperlipidemia in a dose-dependent manner in HFG diet-fed mice compared to the control group. Groups treated with the two reference antidiabetic drugs showed similar values to those treated with aqueous extracts of *E. japonica* leaves. LLE exerts a significant effect against diabetes and excess lipids by regulating blood sugar, insulin, and lipid levels while also providing protection against oxidative stress. Phenolic compounds, including phenolic acids and flavonoids, may play a role in these pharmacological effects.

Additionally, Mogole *et al.* (2020) evaluated the antidiabetic activity of various South African loquat leaf extracts by studying their inhibitory effects on α -amylase. The results showed that all consecutive extracts inhibited α -amylase. Among them, the hexane extract exhibited the highest inhibitory capacity (24%) at a concentration of 1 μ g/mL compared to other extracts. Acarbose, used as a standard, showed 100% inhibitory effects on α -amylase. Despite its relatively low inhibition, the hexane extract demonstrated slight antidiabetic activity, which supports its traditional use. These findings confirm that loquat leaf extracts exert antidiabetic effects by inhibiting the digestive enzyme α -amylase, thereby slowing the glucose absorption and leading to blood sugar stabilization.

Furthermore, the studies conducted by Lin *et al.* (2018) on the antidiabetic activity of *E. japonica* (EJ) flowers extracts collected from Taiwan were carried out using the oral glucose tolerance test (OGTT) and in streptozotocin (STZ)-induced diabetic mice. The results showed that EJ flowers extracts activated the Akt in a time-dependent manner, reaching maximum phosphorylation levels after 60 minutes of treatment, similar to insulin's effect. Groups treated with EJ flowers extracts significantly lowered the blood glucose levels after 30, 60, 90 and 120 min of glucose overload compared to the control group. In STZ-induced diabetic mice, the blood glucose levels and HbA1C proportion increased, while blood insulin levels, which initially reduced, were restored following the EJ flower extracts treatment. Histological analysis revealed that diabetes led to shrinkage and deformation of pancreatic islets in STZ-treated mice compared to control islets. However, treatment with EJ flowers extracts improved the size and shape of these islets. Additionally, skeletal muscle membrane GLUT4 expression, which decreased in STZ-treated mice, significantly increased after EJ flowers extracts administration. Similarly,

C2C12 myotube membrane GLUT4 and p-Akt/tAkt expression levels were elevated in groups treated with insulin, tormentic acid, savinin, euscaphic acid, maslinic acid + corosolic acid, and 2 α ,3 α ,23-trihydroxyolean-12-28-oic acid, compared to the control group. These findings suggest that the EJ flower extracts exert a potent antidiabetic effect through several mechanisms, including activation of the insulin signaling pathway via Akt phosphorylation. This process stimulates the glucose metabolism by enhancing its uptake through GLUT4 transporters. Moreover, these EJ flowers extracts appear to protect pancreatic cells, contributing to improved insulin production. Triterpenes, particularly tormentic acid, euscaphic acid, maslinic acid, corosolic acid, and 2 α ,3 α ,23-trihydroxyolean-12-28-oic acid, are considered the key compounds responsible for these antidiabetic effects.

Biological studies have confirmed the antidiabetic properties of *E. japonica* leaves and flowers, which are primarily attributed to their phenolic acids and flavonoids, as well as to triterpenes contents, respectively. These compounds exert their effects through various mechanisms, including the regulation of blood glucose, insulin, and lipid levels, protection against oxidative stress and pancreatic cell damage, and inhibition of the digestive enzyme α -amylase.

Anti-obesity and hypolipidemic effects

The ethanolic extracts from the leaves, fruits, and seeds of *E. japonica* were examined for their anti-obesity and hypolipidemic effects in Wistar rats with high-fat diet (HFD)-induced obesity. Treatment with various loquat extracts led to a reduction in body weight, creatinine levels, glutamic-oxaloacetic transaminase (GOT), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), total cholesterol (TC), triglycerides (TG), low density lipoproteins (LDL), very low-density lipoproteins (VLDL) and glucose. Additionally, the ethanolic extracts enhanced albumin, total protein, and high-density lipoproteins (HDL) levels compared to the obese control group. These results indicate that the ethanolic extracts from various parts of the loquat tree exhibit significant anti-obesity activity by reducing body weight and blood glucose levels, simultaneously improving the lipid profile, and protecting the liver and kidneys against damages induced by a high-fat diet (Abdelrahman *et al.* 2023). Furthermore, a study by Lee *et al.* (2016) on obese mouse model (induced by high-fat diet) confirmed the anti-obesity effects of *E. japonica* leaves (EJE). Besides promoting a reduction in body weight and lowering TC and TG levels, EJE also contributed to a decrease in leptin levels, unlike the obese group. Moreover, Mansour *et al.* (2022) demonstrated that loquat leaf extract exerts a dose-dependent cytostatic effect against obesity. This mechanism is based on the modulation of inflammatory cytokine levels (IL-6 and TNF- α), leading to a decrease in the differentiation of preadipocytes into mature adipocytes and a reduction in lipid accumulation in the 3T3-L1 cell line. The infectious dose (ID₅₀) values, corresponding to the extract concentration required to reduce adipogenesis and lipid accumulation to a half-maximal (50%), are estimated at 183.7 μ g/mL and 406.9 μ g/mL, respectively. By limiting the production of inflammatory cytokines, this approach contributes to a reduction in inflammation within adipose tissue, stimulating an improvement in metabolic regulation and slowing the development of obesity.

These studies show that *E. japonica* extracts have anti-obesity potential through several mechanisms, including a reduction in body weight via appetite suppression, abating in lipid accumulation and improvement of lipid profile (lower TC, TG, and LDL levels, and higher HDL), regulation of inflammatory cytokines (IL-6 and TNF- α) that influence the adipose tissue inflammation and metabolic processes, as well as hepatic and renal protection against high-fat diet-induced damages.

Cardioprotective effect

The study conducted by Huang *et al.* (2022) examined the cardioprotective effects of polysaccharides extracted from *E. japonica* leaves (EJP). The results revealed that EJP can protect myocytes (H9c2) against hydrogen peroxide (H₂O₂)-induced cell death and may partially help to restore the integrity of their membranes. Additionally, the myocardial ischemia reperfusion injury (MIRI) assay demonstrated that EJP exerts potent concentration-dependent effects in mitigating the myocardial infarction, while significantly reducing the size of the infarcted area. Moreover, EJP contributes to the suppression of risk factors associated with myocardial damage and enhances cardiomyocyte morphology. Its administration also increases the activity of antioxidant enzymes, such as superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), while reducing malondialdehyde (MDA) levels. In parallel, EJP significantly decreases the secretion of inflammatory cytokines TNF- α and IL-6. These results suggest that EJP has a strong cardioprotective potential, primarily due to its antioxidant and anti-inflammatory effects.

In addition to the protective effects of EJP against oxidative stress and myocardial infarction, Chiang *et al.* (2018a) conducted another study to examine the cardioprotective effects of *E. japonica* leaf extract (EJLE) on hypertension-induced apoptosis and fibrosis in spontaneously hypertensive rats (SHR). Echocardiography revealed that EJLE-treated rats exhibited improved cardiac parameters compared to untreated hypertensive rats. Histological analysis demonstrated that EJLE administration

reduced the myocardial apoptosis and fibrosis in the treated groups, unlike in untreated hypertensive rats. Additionally, a decrease in the expression of proteins involved in these pathological processes was observed. EJLE also promotes cardiac cell survival by increasing the expression of markers associated with cell viability in SHR. These findings indicate that EJLE exerts significant cardioprotective activity by attenuating hypertension-induced apoptosis and fibrosis, while improving cardiomyocyte survival.

Building on this research, Chiang *et al.* (2018b) further examined the effects of EJLE by investigating its impact on angiotensin II (Ang II)-induced cardiac hypertrophy in H9c2 cardiomyoblasts and SHR. The results revealed that EJLE supplementation reduced the expression of key mediators of cardiac hypertrophy, including AT1R, MEL-18, HSF2, IGF-IIR, p-MEK, calcineurin, GATA-4, p-GATA4, NFATc3, and BNP, while enhancing the cardiac structure and functions. These observations suggest a potent cardioprotective effect of EJLE that is achieved through modulation of signaling pathways associated with this pathology and improvement of the heart's morphological and functional characteristics.

Studies have also confirmed the cardioprotective properties of *E. japonica* extracts, which act through distinct mechanisms. EJP provides protection primarily through its antioxidant and anti-inflammatory effects, limiting myocyte oxidative stress and reducing the secretion of pro-inflammatory cytokines. Conversely, EJLE primarily enhances cell viability and cardiac functions, with targeted action on apoptosis, fibrosis, and myocardial hypertrophy, helping to preserve cardiac tissue more effectively.

While *E. japonica* extracts have demonstrated significant cardioprotective effects, other studies investigated the impact of different extracts from this plant on the cardiovascular and metabolic health. In this context, Mokhtari *et al.* (2023) analyzed the effects of aqueous fruit peel extracts on lipid and glycemic parameters in mouse models. When administered at doses of 100 or 200 mg/kg BW, these extracts significantly reduced the TC, TG, LDL cholesterol, atherogenic index, LDL-C/HDL-C ratio, and plasma glucose, while promoting an increase in HDL cholesterol. These findings suggest that fruit peel extracts may serve as potential therapeutic agents for the management of diabetes and cardiovascular diseases.

Bronchodilatory and relaxation effects on the tracheal smooth muscles

The relaxing effects of the ethanolic extracts of loquat leaves (EEEJL) was carried out by Marianne *et al.* (2021) on isolated guinea pig trachea. The results showed that the extract exhibited a dose-dependent relaxant effect on histamine-precontracted tracheal smooth muscles. The maximum relaxation ($73.86 \pm 15.35\%$) was achieved at a concentration of 8 mg/mL. EEEJL induced relaxant effects by inhibiting phosphodiesterase-5 (PDE-5) and acting as a noncompetitive antagonist of the histamine-1 (H-1) receptors. The bronchodilatory effects of this extract were further confirmed by a study conducted by Marianne *et al.* (2018) on an isolated strip of guinea pig trachea pre-contracted with acetylcholine (ACh). The results showed that EEEJL induced relaxation, with an effective concentration 50 (EC_{50}) of 1.36 mg/mL, through the inhibition of phosphodiesterase (PDE) and the protection of PGE_2 . These studies collectively demonstrate that the ethanolic extract of loquat leaves exerts a potent bronchodilatory effect by inhibiting the PDE and the H-1 receptor, while protecting the PGE_2 .

Neuroprotective effect

Bae and coworkers evaluated the neuroprotective effects of combining ethanol extract of *E. japonica* (EJ) leaves with aqueous extract of *Salvia miltiorrhiza* (SM) roots. Their findings showed that this mixture significantly prevented A β 1-42-induced toxicity ($81.31 \pm 5.73\%$) and caspase-3 activity ($81.31 \pm 6.54\%$). Additionally, it inhibited CoCl₂-induced hypoxia ($81.31 \pm 5.73\%$) and corticosterone-induced deficiency ($76.32 \pm 6.54\%$) in SH-SY5Y cells. In the Morris water maze model, administration of the mixture markedly preserved the spatial learning and memory, protecting against impairments caused by A β 1-42 injection. Moreover, behavioral deficits were attenuated following treatment. These results indicate that the EJ-SM combination exerts synergistic neuroprotective effects against A β 1-42-induced toxicity, suggesting its potential as an effective agent against the associated neuronal damage (Bae *et al.* 2014, Savaliram & Rahul 2024).

Furthermore, the neuroprotective effects of the ethanolic extract of *E. japonica* leaves was confirmed by the study conducted by Kim *et al.* (2011). Their study results demonstrated that pretreatment with this extract inhibited neuronal cell death induced by A β 1-42 peptide injection, while reducing the intracellular accumulation of reactive oxygen species (ROS). Additionally, the extract improved cognitive dysfunction in mice treated with A β 1-42 peptide. These observations highlight its protective effects against oxidative stress and cognitive deficit associated with A β 1-42 peptide. On the other hand, the neuroprotective activity of the hydroalcoholic extract from loquat flowers was evaluated in Parkinsonian rats induced by 6-hydroxydopamine. The study showed that pretreatment with this extract, combined with voluntary exercise, protected the treated group from toxicity induced by 6-hydroxydopamine and Parkinson's disease (Fallah-Mohammadi *et al.* 2014). These

results were confirmed by Shirvani *et al.* (2017), who observed that the injection of the *E. japonica* flower extract (EJFE) increased the cerebral dopamine neurotrophic factor (CDNF) levels and SOD activity, while reducing MDA levels in the cerebral cortex of Parkinsonian rats. Thus, the neuroprotective effect of EJFE may be attributed to the increased levels of SOD and CDNF.

This research highlights the promising therapeutic potential of *E. japonica* extracts in the management of neurodegenerative diseases through the modulation of specific biological pathways. The combination of the ethanolic extract of loquat leaves with the aqueous extract of *Salvia miltiorrhiza* provides protection against amyloid toxicity, mitigates oxidative stress, and enhances cognitive functions. Additionally, the hydroalcoholic extract of loquat flowers promotes the expression of essential neurotrophic factors, enhances antioxidant enzyme function, and protects dopaminergic neurons against degeneration, potentially through CDNF activation and oxidative stress reduction.

Reproductive effects

Oral administration of an aqueous extract of loquat leaves collected from Lebanon showed contraceptive activity in male Balb/c mice, by reducing sperm motility, viability, count, and testosterone and progesterone levels. It also inhibited steroidogenesis and increased prolactin levels. These anti-fertility effects were found to be reversible 20 days after stopping treatment with the extract (Al Moubarak *et al.* 2020). In contrast to these findings, a study conducted by Syafruddin *et al.* (2021) on alloxan- induced diabetic rats (*Rattus norvegicus*) showed that *E. japonica* leaves improved spermatogenesis by preserving the number of spermatozoa destroyed by diabetes. These contradictory results suggest that *E. japonica* leaves contain both contraceptive and reproductive-promoting compounds or that they exert an adaptive effect on fertility depending on the physiological state of individuals. In healthy subjects, they induce a contraceptive effect, whereas in diseased individuals, they stimulate reproduction to compensate for the damage caused by the condition.

Antidiarrheal activities

The antidiarrheal effects of the ethanolic extract of *E. japonica* leaves (EEJ) were evaluated in Sprague Dawley rats of two genera using three experimental methods: a diarrhea test, enteropooling induced by castor oil administration, and a gastrointestinal motility test. The results showed that EEJ administration at doses 100, 200, and 400 mg/kg BW inhibited the diarrhea induced by castor oil in a dose-dependent manner by 38.1, 76.19 and 100%, respectively. EEJ was also effective in reversing the enteropooling, reducing the volume of intestinal contents by 24.37, 43.29 and 79.83%, respectively and the weight of intestinal contents by 26.82; 45.8 and 78.41%, respectively. Additionally, EEJ decreased gastrointestinal motility by 28, 62 and 84%, respectively. At 400 mg/kg BW dose, these effects were comparable to the reference drug loperamide but were reversed in the group pre-incubated with yohimbine. This study demonstrated the efficacy of EEJ against diarrhea by stimulating α_2 adrenergic receptors and modulating the Na⁺/K⁺-ATPase and NO pathways (Kamadyaapa *et al.* 2018).

Hepatoprotective effects

The hepatoprotective effects of methanol extract (Er1), ethyl acetate fraction (Er2), butanol fraction (Er3) and water fraction (Er4) from *E. japonica* leaves grown in Egypt were evaluated in male albino rats with hepatic lesions induced by subcutaneous injection of carbon tetrachloride (CCl₄). Changes in biochemical parameters revealed that administration of Er1, Er2, Er3 and Er4 at a dose of 250 or 500 mg/kg BW significantly reduced the levels of ALT, AST, alkaline phosphate (AP), GGT, and bilirubin compared to the positive control group. However, the cholesterol, TG, LDL, HDL, and VLDL remained unaffected. All groups treated with loquat extracts, at both low or high doses, except those receiving Er1 and Er4 at low doses, showed a reduction in MDA levels. Additionally, the Er-2 and Er-3 increased levels of nonprotein sulfhydryl groups (NP-SH) and total protein unlike the positive control group. Histological analysis proved that Er2 at a dose of 500 mg/kg BW resulted in excellent hepatoprotection, maintaining normal lobules and hepatocytes, while other extracts also contributed to liver improvement against CCl₄-induced hepatotoxicity. These results suggest that loquat leaf extracts may have a hepatoprotective effect, enhancing liver function and reducing oxidative stress (Shahat *et al.* 2018). This hepatoprotective activity is further supported by a study conducted by Yan *et al.* (2023), which demonstrated that ethanolic extracts of loquat fruit peels and flesh contain 22 phenolic compounds and 2 terpenoid compounds. These extracts were found to effectively improve liver damage caused by alcohol consumption.

Moreover, total sesquiterpene glycosides (TSG) isolated from loquat leaves harvested in China were evaluated for their pharmacological effects against HFD-induced non-alcoholic fatty liver disease (NAFLD) in mice. The mice were fed either a normal diet or HFD for eight weeks. During the last four weeks of the experiment, TSG (25 and 100 mg/kg BW/day), and simvastatin (10 mg/kg BW/day) were administered orally. The results demonstrated that TSG reduced body weight, fat deposition in the liver, and TC and TG levels in NAFLD mice. In addition, TSG decreased the expression of SOD, ALT,

cytochrome P450 2E1 (CYP2E1), and c-jun N-terminal kinase (JNK) phosphorylation, while increasing the MDA levels at 100 mg/kg BW/day, exhibiting excellent effects against NAFLD (Jian *et al.* 2017). These results align with the findings of Yoshioka *et al.* (2010), who reported that ethanolic extracts of *E. japonica* seeds inhibited non-alcoholic steatohepatitis induced by lipid accumulation in the liver. Collectively, these studies indicate that *E. japonica* exerts strong hepatoprotective effects by modulating lipid metabolism and alleviating oxidative stress.

In another study Jiang *et al.* (2017) investigated the effects of tormentic acid (TA), isolated from cell suspension cultures of *E. japonica* against hepatotoxicity induced by intraperitoneal administration of acetaminophen (APAP) in mice. Intraperitoneal pre-administration of TA effectively inhibited the increase in ALT, AST, total bilirubin (T-Bil), TC, TG, and hepatic lipid peroxides, similar to the effects observed in the N-acetylcysteine (NAC) positive control group. Histological analysis showed that TA pre-administration improved morphological damages induced by APAP. Additionally, TA reduced the production of NO, and ROS, as well as the protein expression of iNOS and COX-2. The results suggest that TA may help to mitigate oxidative stress and inflammation by enhancing the antioxidant protein HO-1 and maintaining the key antioxidant enzymes, including glutathione peroxidase (GPx), catalase (CAT) and SOD. In addition to inhibiting the release of three inflammatory mediators: interleukin-1beta (IL-1 β), IL-6 and TNF- α . TA suppresses the phosphorylation of mitogen activated protein kinases (MAPK) and NF- κ B. It has a strong ability to prevent the hepatocytes from damage by reducing inflammation and oxidative stress (Chang *et al.* 2011, Li *et al.* 2017b, Olech *et al.* 2021).

The various extracts and compounds tested have demonstrated that *E. japonica* exhibits remarkable hepatoprotective activity, acting through multiple mechanisms. These effects include enhancing liver functions, reducing inflammation and oxidative stress, and regulating lipid metabolism.

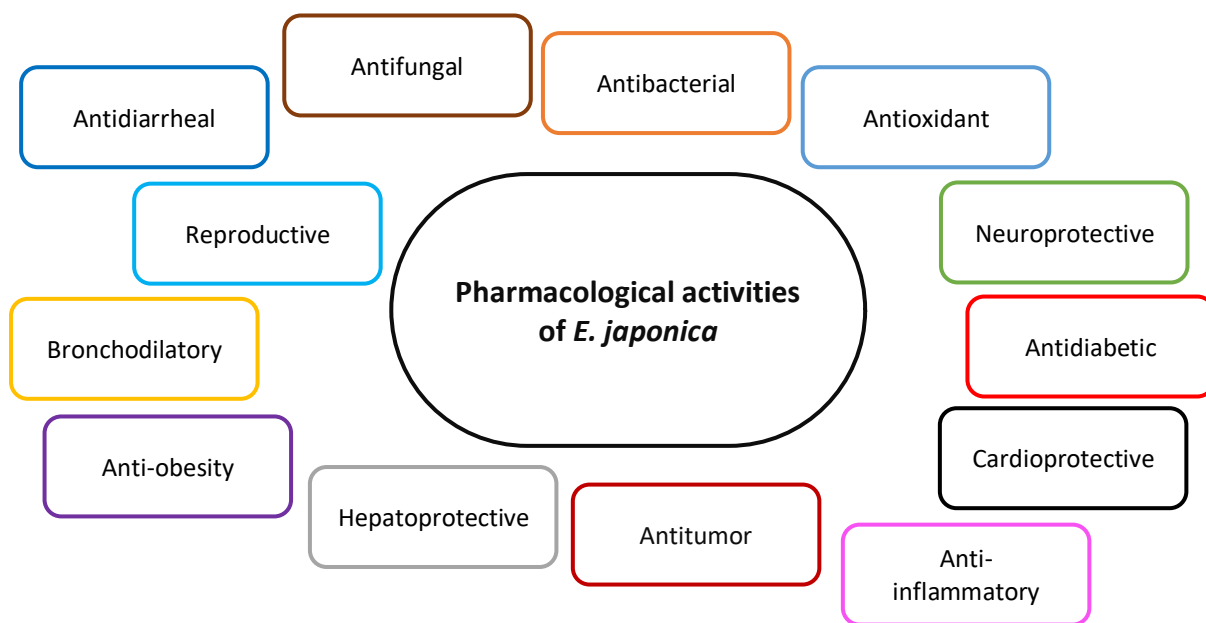


Figure 5. Pharmacological activities of *E. japonica*.

Toxicology of *E. japonica*

The acute toxicity tests of the aqueous extracts of loquat leaves (LLE) grown in Morocco have been carried out on mice. The results demonstrated that the body weight of the groups treated with different doses of LLE (500 to 5000 mg/kg BW) was like the control group. No signs of toxicity or mortality were observed during the 14 days of treatment. The median lethal dose (LD₅₀) was found to be greater than 5000 mg/kg BW (Khouya *et al.* 2022). Additionally, the oral administration (by gavage) of triterpene acid isolated from the leaves of *E. japonica* (ELTA) caused neither mortality nor toxicity in ICR mice in the acute phase and also in subacute treatment (Li *et al.* 2017a). Finally, after 13 weeks of repeated treatments with three separate oral doses (250, 500 and 1000 mg/kg BW/day) of loquat leaf extract, no adverse effects were observed in all the three groups. It was concluded that the dose with any harmful effects should therefore be higher than 1000 mg/kg BW/day (Seong *et al.* 2018).

Discussion

The biological effects of *E. japonica* are attributed to its bioactive compounds, which provide a remarkable chemical diversity. Among these substances, polyphenols contribute to antioxidant, antimicrobial, antitumor, antidiabetic, hepatoprotective, bronchodilatory, and reproductive properties. Triterpenes, on the other hand, play a key role in anti-inflammatory, antitumor, and antidiabetic functions, while polysaccharides are primarily involved in cardioprotective and tumor-suppressing effects. The presence of carotenoids, such as β -carotene and β -cryptoxanthin, lutein, violaxanthin, α -carotene and γ -carotene have been shown to protect against certain disease conditions (De Almeida Lopes *et al.* 2018).

Phenolic compounds are powerful natural antioxidants that neutralize free radicals, transfer electrons and hydrogen atoms, and chelate with metal cations to excrete them from the body. Their efficacy is determined by their molecular structure, particularly the number and position of hydroxyl groups, as well as the nature of the substituents on the aromatic rings. Flavonoids, a subclass of polyphenols, play a crucial role in protecting LDL from oxidation, thereby helping to prevent lipid peroxidation. Their mechanism of action relies on their ability to neutralize free radicals such as superoxides, lipid peroxides, and hydroxylated compounds. Additionally, they inhibit lipoxygenase activity and inactivate oxygen molecules. The remarkable effectiveness of flavonoids is attributed to their ability to transfer a hydrogen atom from a hydroxyl group to free radicals, ensuring their stabilization and limiting oxidative damage (Hassanpour & Doroudi 2023, Tumilaar *et al.* 2024).

In addition to their strong antioxidant effects, polyphenols play a crucial role in defense against pathogens. Their antimicrobial activity relies on several complementary mechanisms, including inhibition of quorum sensing, interaction with cell membranes, enzyme inhibition, ROS generation, and metal ion binding (De Rossi *et al.* 2025). By disrupting the quorum signals, they alter the gene expression of microorganisms, disintegrate the bacterial aggregation and prevent the formation of biofilms (Mohanty *et al.* 2023, Moreno-Gómez *et al.* 2023, Nguyen *et al.* 2024). Additionally, they enhance the host immune response, contributing to better protection against microbial infections. Their interaction with cell membranes affects the permeability and modifies the membrane proteins, triggering ROS production because of membrane disruption. These ROS cause structural damages that compromise membrane integrity and functionality, ultimately leading to cell lysis. This results in intracellular leakage, impairing the microbial biological functions. However, the specific mechanisms may vary depending on the target microorganism, the molecular structure of polyphenols, and environmental conditions (Davidova *et al.* 2024).

Beyond their antimicrobial properties, polyphenols also play a crucial role in cancer prevention and treatment through multiple biological mechanisms. Their antitumor activities are primarily associated with their ability to inhibit cell proliferation, induce apoptosis, activate autophagy, and regulate the cell cycle. Additionally, they prevent tumor cell migration and invasion, reduce angiogenesis, and influence epigenetic and metabolic pathways (Farghadani & Naidu 2023). Their anticancer potential stems largely from their antioxidant properties, allowing them to neutralize free radicals, chelate metals, and modulate endogenous defense systems such as SOD, CAT, GPx, and GSH. Furthermore, polyphenols regulate key proteins and transcription factors involved in cancer progression, while limiting tumor growth by inhibiting polyamine biosynthesis and cell signaling enzymes. As a result, they play a significant role in modulating the expression of proteins essential for cell cycle regulation, metastasis prevention, and programmed cell death (Chimento *et al.* 2023).

Alongside their anticancer properties, polyphenols play a crucial role in the prevention and management of diabetes due to their diverse biological effects. They protect pancreatic cells from glucose toxicity, support their proliferation, and reduce apoptosis, which enhances insulin secretion. Moreover, these compounds inhibit digestive enzymes such as α -amylase and α -glucosidase, slowing glucose absorption and helping to stabilize blood sugar levels. Their potent antioxidant and anti-inflammatory activities mitigate oxidative stress and insulin resistance, while modulating carbohydrate and lipid metabolism. Polyphenols also stimulate insulin signaling, promoting efficient glucose utilization by cells. Furthermore, they regulate the intestinal microbiota, enhance adipose tissue metabolism, and inhibit the formation of advanced glycation end products, which contribute to diabetic complications (Naz *et al.* 2023, Shahidi & Danielski 2024).

Polyphenols exert protective effects on the liver and display anti-hepatocarcinogenic effects through multiple mechanisms. They modulate lipid and glucose metabolism, influence mitochondrial function, reduce oxidative stress, while aiding in the clearance of toxic metabolites and contribute to hepatic homeostasis. Additionally, they play a key role in regulating hepatic inflammation, further reinforcing their therapeutic value for liver health (Gajender *et al.* 2023, Li *et al.* 2023).

Because of their structural similarity to estradiol, polyphenols can exert estrogenic activity, influencing the reproductive functions. Through their antioxidant properties, they positively impact the reproductive health by enhancing the quality of

male and female gametes. Epigallocatechin-3-gallate, a polyphenol, primarily regulates ROS, optimizing enzyme activity, supporting germ and oocyte cells, and strengthening antioxidant defenses. Additionally, it helps to reduce sperm malformations and improves the overall health of the male and female reproductive systems (Bešlo *et al.* 2022). Resveratrol, another polyphenol with reproductive potential, plays a crucial role in addressing age-related infertility. Its actions on mitochondrial membrane potential, oxidative stress reduction, and inflammation control are of particular significance. Moreover, it may alleviate the symptoms of polycystic ovary syndrome by lowering androgen levels, reducing inflammation and fibrosis, through enhancing metabolism, fertility, and ovarian and oocyte morphology. It also helps to regulate the menstrual cycle, further reinforcing its protective effects on reproduction (Podgrajsek *et al.* 2024).

In addition to polyphenols, triterpenes are the bioactive compounds with multiple pharmacological effects. They exhibit potent anti-inflammatory potential through several mechanisms of actions and are considered as strong candidates for the development of anti-rheumatic drugs (Faustino *et al.* 2023). They reduce oxidative stress by limiting the production of ROS and inhibit the secretion of pro-inflammatory mediators such as TNF- α , interleukins (IL-1 β and IL-6), and PDE₂. Moreover, they suppress the expression of COX-2 and iNOS, and attenuate the translocation of the p65 subunit of the NF- κ B transcription factor to the nucleus, thereby modulating the inflammatory and immunomodulatory responses (De Santana Souza *et al.* 2014, Han & Bakovic 2015, Huang *et al.* 2011, Renda *et al.* 2022).

Similar to polyphenols, triterpenoids also play a key role in cancer prevention and treatment through several mechanisms. They promote apoptosis and exhibit cytotoxicity against various types of tumor cells by targeting intrinsic and extrinsic pathways, disrupting the mitochondrial integrity, cell cycle and epigenetics/epigenomics regulations and modulating the cell death regulatory proteins (Li *et al.* 2020c, Moralev *et al.* 2024). Furthermore, they inhibit tumor cell proliferation and growth by altering the cell cycle, regulating signaling pathways, and inducing cellular stress, leading to a reduction in tumor mass. Additionally, they exert an antiangiogenic effect, limiting the formation of new blood vessels and thus slowing tumor progression. Their anti-metastatic potential is expressed through the inhibition of cancer cell invasion, interference with receptor signaling pathways, regulation of the epithelial-mesenchymal transition, and suppression of matrix metalloproteinases. Triterpenoids have also been shown to possess potent anti-ulcer properties and are embroiled in pathways associated with inflammation, oxidative stress, apoptosis, and mucosal protection (Shen *et al.* 2025). They regulate the inflammatory and immune responses by influencing the activity of immune cells such as T lymphocytes and Natural Killer cells, thereby enhancing anticancer immunity (Aly *et al.* 2024, Lee *et al.* 2024). Like polyphenols, triterpenes exhibit strong antidiabetic properties by blocking the enzymes involved in insulin resistance, promoting glucose metabolism, and regulating plasma glucose and insulin levels (Shivam *et al.* 2023).

Flavonoids play a crucial role in preventing the respiratory diseases through their diverse biological actions. They help to limit inflammation, reduce oxidative stress, and inhibit cellular senescence, thereby preserving lung tissue health. Additionally, these compounds restore corticosteroid sensitivity, improve lung histology, and enhance the respiratory functions through modulation of key signaling pathways and molecular targets (Yang *et al.* 2020). Moreover, flavonoids inhibit respiratory infections, prevent excessive extracellular matrix deposition, and contribute to tumor growth regulation in various lung diseases (Jing *et al.* 2021). Higher dietary intakes of flavonoids have been shown to improve the lung functions as they lower the risk of chronic obstructive pulmonary disease and asthma, even in smokers (Bondonno *et al.* 2024). Their therapeutic potential positions them as promising agents in the prevention and treatment of chronic respiratory conditions (Wu *et al.* 2024).

Polysaccharides are another class of bioactive compounds that exert cardioprotective effects through several mechanisms. They reduce oxidative stress, support the metabolism of biological macromolecules, and regulate the apoptotic cascade to reduce excessive cell apoptosis. Additionally, they inhibit inflammatory signaling pathways, contributing to the reduction of inflammation. Furthermore, they promote NO production, enhancing vasodilation and protecting against endothelial dysfunction, thereby improving cardiovascular functions (Dong *et al.* 2021). Loquat peel polysaccharides have been shown to possess significant antioxidant and antihyperglycemic properties (Liu *et al.* 2025). The majority of polysaccharides also exert their anticancer effects by inducing cell cycle arrest, anti-angiogenesis, apoptosis, and immunomodulation, while reducing oxidative stress (Guo *et al.* 2022, Ying & Hao 2023).

Conclusion and perspectives

This review provides a comprehensive summary of the botany, ecology, phytochemistry, and biological activities of *E. japonica*. It also provides some practical support and ideas for future studies that should be conducted on this plant. Loquat is consumed as a fruit as well as in the development of value-added food products and is also used in various traditional

medicine practices. The pharmacological studies listed here cover almost all the ethnomedicinal uses of this plant, highlighting its potential in a range of pharmacological areas, including antidiabetic, cardioprotective, anticancer, antimicrobial, hepatoprotective activities, and many other healing properties. A closer look at the phytochemical composition of different parts of this plant reveals a rich diversity of biochemical compounds that may be responsible for its bioactive potential. It would therefore be interesting to focus on its bio-guided fractionations to isolate and purify the bioactive chemical components. In addition to this, the mechanism of action, bioavailability and pharmacokinetics of these bioactive ingredients will be of great significance when assessing their pharmacological effects. Another important feature that contributes to the development of this plant species is to study its nutrigenomic effects in mouse models.

Declarations

List of abbreviations: ABTS - 2,2'-Azinobis (3-ethylbenzothiazoline-6-sulfonic acid); Ach - Acetylcholine; ADP - Adenosine Diphosphate; ALP - Alkaline Phosphatase; ALT - Alanine Aminotransferase; AMP - Adenosine Monophosphate; Ang-II - Angiotensin II; AP - Alkaline Phosphate; APAP - Acetaminophen; AR - Androgen Receptor; AST - Aspartate Transaminase; ATP - Adenosine Triphosphate; *B. cereus* - *Bacillus cereus*; BW - Body Weight; CAT - Catalase; CCl₄ - Carbon Tetrachloride; CDNF - Cerebral Dopamine Neurotrophic Factor; CFA - Complete Freund's Adjuvant; CH₂Cl₂ - Dichloromethane; COX-2 - Cyclooxygenase-2; CYP2E1 - Cytochrome P450 2E1; DCF - Dichlorofluorescein; DMBA - 7,12-Dimethylbenz[α]anthracene; DPPH - 1,1-Diphenyl-2-picrylhydrazyl; EBV-EA - Epstein-Barr Virus Early Antigen; EC₅₀ - Effective Concentration 50; *E. deflexa* - *Eriobotrya deflexa*; EEEJL - Ethanolic Extract of *Eriobotrya japonica* Leaves; EJ - *Eriobotrya japonica*; *E. japonica* - *Eriobotrya japonica* (Thunb.) Lindl.; EJCE - *Eriobotrya japonica* Culture Extract; EJE - *Eriobotrya japonica* Extract; EJFE - *Eriobotrya japonica* Flower Extract; EJLE - *Eriobotrya japonica* Leaf Extract; EJP - Polysaccharide isolated from *Eriobotrya japonica*; EJP90-1 - *Eriobotrya japonica* Polysaccharide 90-1; EJP90-1-Se - *Eriobotrya japonica* Selenylation-modified Polysaccharide; ELTA - *Eriobotrya japonica* Leaves Triterpene Acid; *E. prnoides* - *Eriobotrya prnoides*; Er1 - Methanol Extract of *Eriobotrya japonica* Leaves; Er2 - Ethyl Acetate Fraction of *Eriobotrya japonica* Leaves, Er3- Butanol Fraction of *Eriobotrya japonica* Leaves; Er4 - Water Fraction of *Eriobotrya japonica* Leaves; EtOAc - Ethyl Acetate; FAOSTAT - Statistical database of the Food and Agriculture Organization of the United Nations; FASN - Fatty Acid Synthase; FRAP - Ferric Reducing Antioxidant Power; FW - Whole Fruit; GAE - Gallic Acid Equivalent; GGT - Gamma-Glutamyl Transferase, GLUT4 - Glucose Transporter 4; GOT - Glutamic-Oxaloacetic Transaminase; GPx - Glutathione Peroxidase; H-1 - Histamine-1; HbA1C - Glycated Hemoglobin; HDL - High Density Lipoproteins; HeL - Hexane Extract from the Leaves; HepG2 - Tumor Cells; HFD - High-Fat Diet; HFG - Diet High in Fat and Glucose; H₂O₂ - Hydrogen Peroxide; HPLC - High-Performance Ion-exchange Chromatography; HPLC-DAD - High Performance Liquid Chromatography System with Diode Array Detector; HPLC-ESI-MS - High Performance Liquid Chromatography Coupled with Electrospray Ionization Mass Spectrometry; HR-ESI-MS - High-Resolution Electrospray Ionization Mass Spectrometry; IC₅₀ - Median Inhibitory Concentration; ID₅₀ - Infectious Dose 50; IL-1 β - Interleukin-1beta; IL-6 - Interleukin-6; iNOS - Inducible NO Synthase; JNK - c-Jun N-terminal Kinase; LD₅₀ - Median Lethal Dose; LDL - Low Density Lipoproteins; LEJ - *Eriobotrya japonica* Leaves; LLE - Loquat Leaves Extract; LSS - Loquat Seed Starch; MAPK - Mitogen Activated Protein Kinases; MDA - Malondialdehyde; MeOH extract - Methanolic extract; MeS - Methanol Extract from the Seeds; MFC - Minimum Fungicide Concentration; MIC - Minimum Inhibitory Concentration; MIRI - Myocardial Ischemia Reperfusion Injury; MTT - 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide; NAC - N-Acetylcysteine; NAFLD - Non-alcoholic Fatty Liver Disease; n-BuOH - n-Butanol; NF- κ B - Nuclear Factor-Kappa B; NMR-MS - Nuclear Magnetic Resonance-Mass Spectrometry; NO - Nitric Oxide; NP-SH - Non-Protein Sulfhydryl; OGTT - Oral Glucose Tolerance Test; PCa - Prostate Cancer; PDE-5 - Enzyme Phosphodiesterase-5; *P. digitatum* - *Penicillium digitatum*; PGE₂ - Prostaglandin E₂; PSA - Prostate Specific Antigen; QE - Quercetin Equivalent; RI - Ripe Loquat; ROS - Reactive Oxygen Species; SC₅₀ - 50% Scavenging Concentration; SHR - Spontaneously Hypertensive Rats; SOD - Superoxide Dismutase; SREBP-1 - Sterol Regulatory Element-Binding Protein-1; *S. aureus* - *Staphylococcus aureus*; STZ - Streptozotocin; TA - Tormentic Acid; TBA - 2- Thiobarbituric Acid; T-Bil - Total Bilirubin; TC - Total Cholesterol; TE - Trolox Equivalent; TG - Triglycerides; TNF- α - Tumor Necrosis Factor-alpha; TPA - 12-O-tetradecanoylphorbol-13-acetate; TSG - Total Sesquiterpene Glycosides; UHPLC-DAD - Ultra-High Performance Liquid Chromatography with Diode Array Detector; UNR - Unripe Loquat; UNS - Unripe Starch; UPLC-Q-TOF-MS - Ultra-Performance Liquid Chromatography Quadrupole-Time-Of-Flight Mass Spectrometry; VLDL - Very Low Density Lipoproteins.

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