



REVIEW ARTICLE

Bioactivities of *Prunus mahaleb*: A Mini Review

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ARTICLE HISTORY

Received: 08 March 2023

Accepted: 29 March 2024

Available online

Version 1.0 : 12 May 2024



Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

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Publisher's Note: Horizon e-Publishing Group remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Indexing: Plant Science Today, published by Horizon e-Publishing Group, is covered by Scopus, Web of Science, BIOSIS Previews, Clarivate Analytics, NAAS, UGC Care, etc See https://horizonepublishing.com/journals/index.php/PST/indexing_abstracting

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CITE THIS ARTICLE

Ibrahim NM, Abdul-jalil TZ, Mahmood AS. Bioactivities of *Prunus mahaleb*: A Mini Review. Plant Science Today (Early Access). <https://doi.org/10.14719/pst.2492>

Abstract

The mahaleb cherry, which has the scientific name *Prunus mahaleb* L., is a fragrant shrub plant belonging to the Rosaceae family. The plant is commonly cultivated in the Mediterranean area. The people cultivated it for its essential oil and seeds, which have great therapeutic and nutritional value. It is widely distributed over North Africa, Central Asia, and Central-South Europe. The plant contains a variety of active constituents like coumarins, vital oils, polyphenolic ingredients, and other phytochemical compounds that possess many pharmacological activities capable of improving people's health. These activities include antioxidant, antimicrobial, anti-inflammatory, gastro-protective, neuroprotective, and diabetic management actions. Overall data for this literature review was collected from online sources such as Google Scholar, Science Direct, Scopus, Research Gate, Elsevier, PubMed, and Web Science. In addition to that, the library of the pharmacognosy department was utilized to collect supplementary information on photochemical constituents, pharmacognosy, and pharmacological applications of mahaleb cherry. The gathered data was carefully examined and authenticated. The main aim of this review article is to uncover potential therapeutic activities of this plant that could be valuable in the future for therapeutic nutrition, as well as food and pharmaceutical industries.

Keywords

Antioxidant; Bioactivity; Edible oil; Polyphenol; *Prunus mahaleb*

Introduction

The small tree of *Prunus mahaleb* L. grows and reaches 10 meters in height. This deciduous shrub plant has white blooms and dark brown bark. The original distribution of *Prunus mahaleb* was in Central-South Europe, North Africa, and up to Central Asia (1,2). *Prunus mahaleb* L. seeds are widely known by local names as mahaleb, endulus, mahlep, or mistaka, and having a special taste and odor, the seeds are commonly used in bakery (3). Mahaleb cherries have historically been used as diuretics, tonics, digestive aids, sedatives, and antidiabetics; they are also used as a spice in food (3). The plant is abundant in polyphenolic compounds (phenolic acid, flavonoids, and anthocyanins), organic acids, volatile compounds (aldehydes were the predominant amount), and poly-unsaturated fatty acids in addition to minerals, including iron, copper, and zinc. Additionally, cherry fruit pulp contains the original forms of the distinctive fragrance chemicals coumarin and hydrocoumarin (4). The most beneficial effects of this herb are its analgesic and anti-inflammatory properties (5). In addition,

several articles have demonstrated the antibacterial, antioxidant, and antiviral capabilities of *Prunus mahaleb* (6-8), and more recent phytochemical research has identified several compounds having neuroprotective effects (5). The information for this literature review was taken from reputable online sources like Scopus, Google Scholar, Research Gate, Science Direct, Elsevier, PubMed, and Web of Science. Additional data were also received from the library's college pharmacy to find the light and notarize the morphology, distribution, and ethnobotanical importance of *Prunus mahaleb* (*P. mahaleb*), phytochemical ingredients, and pharmacological activities to reveal other rational therapeutic actions. The review aims to highlight *Prunus mahaleb* L's bioactivities that may promote fresh innovation in pharmaceuticals, foods, and industrial applicants.

Methodology

The data for this literature review were sourced from trustworthy internet platforms such as Scopus, Google Scholar, Research Gate, Science Direct, Elsevier, PubMed, and Web of Science. The search terms used for the medical subheading included "*Prunus mahaleb*", "Anti-bacterial", "Anti-viral", "Anti-fungal", "Antioxidant", "Bioactive compounds", and "Edible oil". The relevant publications were identified based on the titles and abstracts and subsequently retrieved in their entirety. These articles were then checked to ensure their inclusion in this study.

Morphology of the plant

Prunus mahaleb L. is a shrub or small tree that belongs to the Rosaceae family and grows in temperate regions all over the world. Its height ranges from 2 to 10 meters (9). The fruits are typically tiny, spherical, juicy, and flat; they also exhibit a high amount of anthocyanins. When these fruits are fully ripe, their color changes from green to red to black (3, 10). The leaves are wide, alternate, clustered at the ends of twigs that are placed alternately, oblong to cordate, and pointed. Flowers are white, fragrant, and grouped in upright racemes with 3 to 12 flowers that resemble corms (11, 12). The *Prunus mahaleb* seed has a pointed egg form, which serves as a beneficial source of fatty acids (40.40% w/w) and proteins (30.98% w/w) (13), as shown in Figure 1.

Distribution of the plant

The plant is native to the continents and is grown in temperate and tropical climates with well-drained soils. It can withstand hot, dry weather. *Prunus mahaleb* L. is a type of cherry tree that has white blooms and produces amazing dark red plums. It is also known as the mahaleb cherry, white mahaleb, English cherry, or wild cherry. Originally found in North Africa, Central Asia, and Central-South Europe, it is native to Iran, India, Central and Southern Europe, North Africa, Sudan, Syria, Turkey, Armenia, and Azerbaijan (12-15). It is primarily found in the north and northeast of Iraq, where it can be found in regions that are higher than 600 meters above sea level. Most studies about mahaleb indicate that *Prunus mahaleb* grows in mountain areas, especially in the Zewe-Sulymaniya region of Iraqi Kurdistan (16), As shown in Figure 2.

Ethnobotanical importance of *Prunus mahaleb*

Humans depend on plants to meet their basic needs for food, clothing, medicine, and housing. The study of medicinal plants and their traditional usage has drawn more attention in recent years across the globe (17). *P. mahaleb* cherry trees are often used as rootstock to strengthen and vigor the sweet cherry; this practice is especially widespread in Southern Italy, particularly in the Apulia region (18). Traditional scents, lotions, and liqueurs are also made from the plant (19). Because the kernels of crushed seeds have a distinctive bitter taste, they are employed as flavoring agents in bagels, cakes, and muffins, as well as in traditional medicine as diuretic, antidiabetic, tonic, aphrodisiac, and expectorant agents (7), as shown in Table 1.

Phytochemistry

The main categories of phytoconstituents, including terpenoids (essential oil), polyphenolic compounds (phenolic acids and flavonoids), coumarins, and others, are assembled to form the phytochemical composition of *Prunus mahaleb* L. (18, 27). Table 2 and Figure 3 summarize several phytoconstituents in *Prunus mahaleb* L.



Figure 1. *Prunus mahaleb* L. A: Leaves of *Prunus mahaleb*, B: Tree of *Prunus mahaleb*, C: Fruits of *Prunus mahaleb* (10)

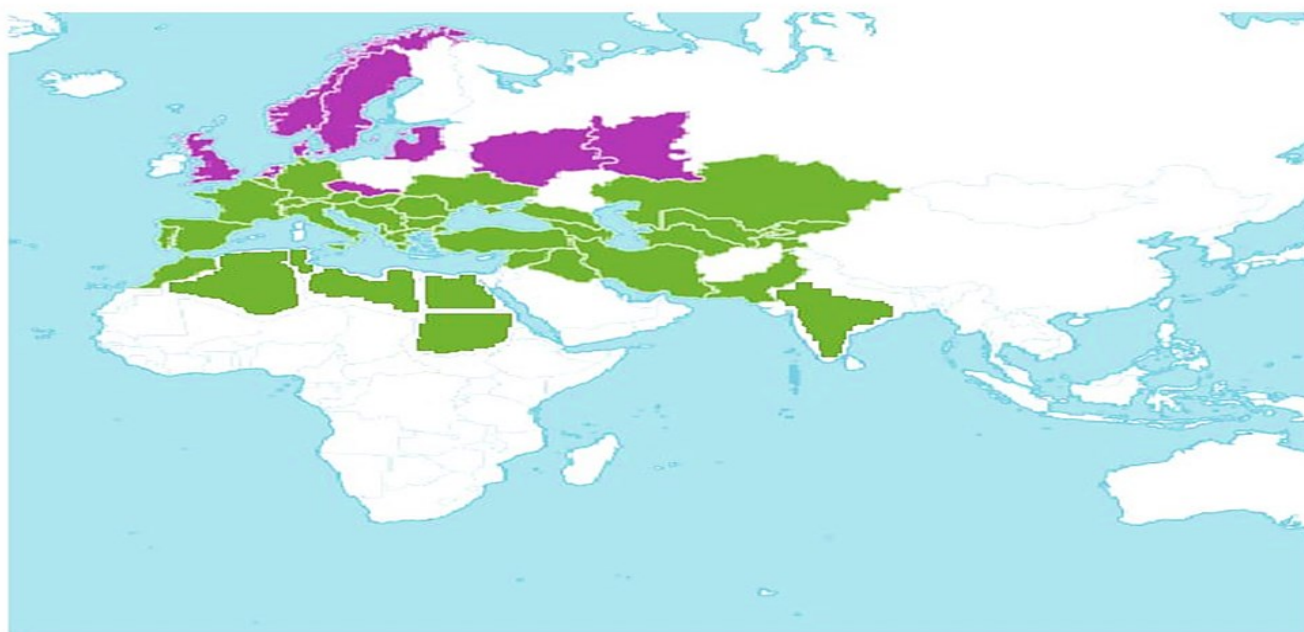


Figure 2. Geographical distribution of *Prunus mahaleb*. All the regions where mahaleb plants are most common are highlighted in green, while the violet color is related to other species of *Prunus* (12,13).

Table 1. Ethnobotanical uses of *Prunus mahaleb*

S.No.	Regions	Part used	Form of use	Ethnobotanical use	References
1.	Middle East and North Africa	Seeds	Powder	An aromatic spice and flavor	20
2.	Sudan	Kernels, seeds	Lotion	Hair nourishing, diarrhea treatment, flavoring agent	6,2,8
3.	Iran	Seed	Extract	kidney stones and respiratory tract infections	21
4.	Turkey	Seeds	Powder	flavoring agent	3
5.	Egypt	Kernels	Powder	Used as tonics, diuretics, digestive aids, sedatives, and antidiabetics	6
6.	Turkey	Kernels	Powder	Improve the quality of bread	22
7.	India	Fruit Kernels	Powder	Reduce hyperpigmentation	8
8.	Iran	Fruit, Wood, Seed	Poultice	Edible as wild fruit, diaphoretic, laxative, culinary and spice, and wild fruit stomachic	23-26
9.	Iraq	Fruit	Powder	Flavor and spice	16

Table 2. The main categories of phytoconstituents in the *Prunus mahaleb* L. plant

S No.	Plant part	Type of compound	Isolated chemical compound	Method of isolation/detection	References
1.	Seeds	Volatile oils	linolenic acid, oleic acid, and linoleic acid	GC-MS	28
2.	Fruits	Phenolic acids	chlorogenic acid, coumaric acid, and ferulic acid	HPLC-DAD-MS	29
4.	Fruits	flavonoids	Rutin, naringenin	HPLC-DAD-MS	8
5.	Fruits, seedcake	Flavan -3-ols	Gallic acid ,catechin and epicatechin	HPLC-DAD-MS	30
	Seeds	Fatty acids & Phthalate esters	phthalate derivatives, six saturated fatty acids, five monounsaturated fatty acids (MUFAs), and three polyunsaturated fatty acids (PUFAs)	GC-MS	27

HPLC-DAD: High-performance liquid chromatography- Diod array detector- Mass spectrometry, **GC-MS:** Gas chromatography – Mass Spectrometry.

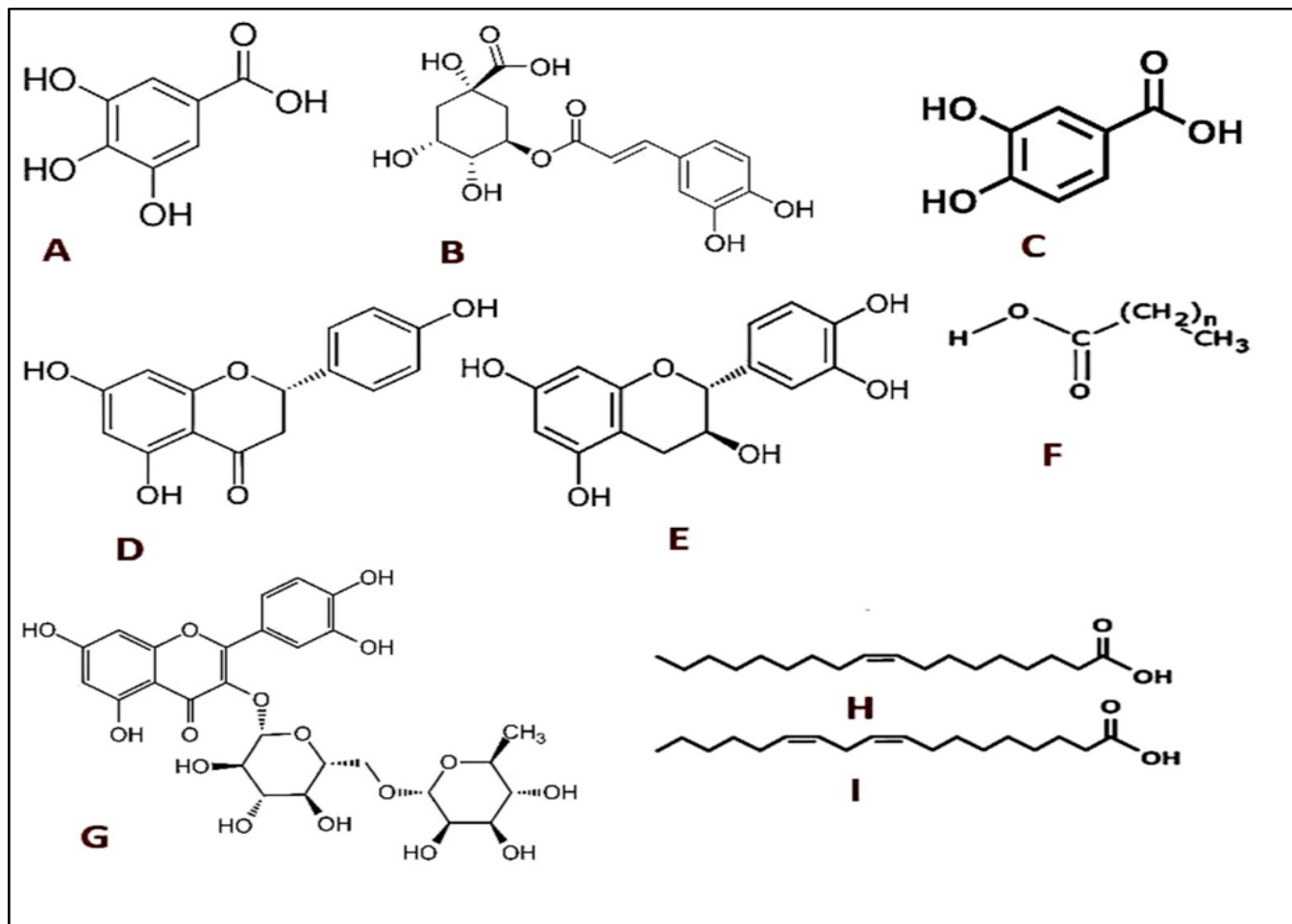


Figure 3. Chemical structure of the main active constituents of *Prunus mahaleb*: A: Gallic acid, B: Chlorogenic acid, C: Protocatechuic acid, D: Naringenin, E: catechin, F: saturated fatty acid, G: Rutin, H: Oleic acid, I: Linoleic acid (26,28, 31-33).

Pharmacological activity of *Prunus mahaleb*

Prunus mahaleb exhibits a range of pharmacological activities, including anti-inflammatory, antibacterial, antiviral, and antifungal effects. These effects can be attributed to the presence of its active constituent, Kernel oil, which contains a high percentage of unsaturated fatty acids (primarily linoleic acid), minerals oil, vitamins, phytosterols, phenolic compounds, carotenoids, and vitamin E (34).

Anti-Inflammatory Activity

The *Prunus mahaleb* plant shows notable anti-inflammatory properties by inhibiting the increased activation of gene expression of tumor necrosis factor- α (TNF- α) and cyclooxygenase-2 (COX-2), primarily in the colon of mice (29). Furthermore, the suppressive impact of the fruit extract of *P. mahaleb* on the production of endothelial adhesion molecules induced by lipopolysaccharide has been assessed in a laboratory setting. The extract exhibits a significant impact even at a concentration of 1 mg/mL, with a 50% drop observed at a concentration of 3 mg/mL. Furthermore, the extract reduces the expression of intercellular adhesion molecules -1 (ICAM-1), vascular cell adhesion molecules-1 (VCAM-1), and E-selectin in a manner that is dependent on the concentration (35).

Anti-bacterial Activity

Along with the increasing resistance of many bacteria to

many types of currently available antibiotics and the high-cost production of many synthetic antibiotics, scientists are constantly searching for novel molecules with antibacterial properties. Herbal plants can be a viable alternative due to their broad safety margin, cost-effectiveness, and efficacy against numerous antibiotic-resistant pathogens. As shown in Table 3, different types of extract (ethanolic, methanolic, and even water) from other parts of the *P. mahaleb* plant (fruit, seed, leaves, branches, and flower) had potential antibacterial activity against various types of gram-positive and gram-negative bacteria like *Bacillus anthracis*, *Staphylococcus aureus*, *Bacillus licheniformis*, *Brucella melitensis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Enterococcus faecalis*, *Vibrio harveyi*, *Bacillus subtilis* and *Proteus mirabilis*. The *Prunus mahaleb* contains a high percent of flavonoid depending on its genotypes with the highest level in fruit (30).

Anti-Fungal activity

The powerful anti-fungal effects of different parts of mahaleb may be related to the plant's capacity to hinder the biochemical manufacturing pathway of aflatoxin, hence impeding fungal growth (39). The methanol extracts derived from seeds, leaves, and fruits have inhibitory properties against many fungus species, including *Candida albicans*, *Candida parapsilosis*, *Candida tropicalis*, and *Candida krusei* (Table 4).

Table 3. Antibacterial activity of different parts of *P. mahlab* extracted in various solvents.

S.No.	Parts used	Type of extract	Bacteria inhibited	Inhibition value	References
1	Flower, leaves, seed kernels, fleshy seed coats, fruit stalks, branches, and resins	Methanolic extract & n-hexane extract	<i>E. coli</i>	32-64 µg/ml	36
2	Fruit	Water extract	<i>E. coli</i>	31.49 µg/ml	37
3	Seed	Ethanol extract	<i>E. coli</i>	Inhibition zone (10-13 mm)	38
4	Flower, leaves, seed kernels, fleshy seed coats, fruit stalks, branches, and resins	Methanolic extract & n-hexane extract	<i>P. aeruginosa</i>	32-64 µg/ml	36
5	Fruit	Water extracts	<i>P. aeruginosa</i>	µg/ml 200<	37
6	Flower, leaves, seed kernels, fleshy seed coats, fruit stalks, branches, and resins	Methanolic extract. & n-hexane extract	<i>P. mirabilis</i>	16 µg µg/ml	36
7	Flower, leaves, seed kernels, fleshy seed coats, fruit stalks, branches, and resins	Methanolic extract. & n-hexane extract	<i>K. pneumonia</i>	32-64 µg /ml	36
8	Flower, leaves, seed kernels, fleshy seed coats, fruit stalks, branches, and resins	Methanolic extract & n-hexane extract	<i>A. baumannii</i>	8-16 µg µg/ml	36
9	Leaves, seed kernels, fleshy seed coats, stalks, and resins	Methanolic extract & n-hexane extract	<i>S. aureus</i>	32 µg/ml	36
10	Flower	Methanolic extract	<i>S. aureus</i>	64 µg µg/ml	36
11	Fruit	n-hexane extract	<i>S. aureus</i>	64 µg µg/ml	36
12	Branches	n-hexane extract	<i>S. aureus</i>	64 µg µg/ml	36
13	Seed	Ethanol extract	<i>S. aureus</i>	Inhibition zone 9 mm	36
14	Flower, leaves, seed kernels, fleshy seed coats, fruit stalks, branches, and resins	Methanolic extract & n-hexane extract	<i>E. faecalis</i>	32 µg µg/ml	36
15	Leaves, seed kernels, fleshy seed coats, fruit stalks, branches, and resins	Methanolic extract & n-hexane extract	<i>E. faecalis</i>	32 µg µg/ml	36
16	Flower	Methanolic extract	<i>E. faecalis</i>	64 µg µg/ml	36
17	Flower, leaves, seed kernels, fleshy seed coats, fruit stalks, branches, and resins	Methanolic extract & n-hexane extract	<i>B. subtilis</i>	16 µg µg/ml	36
18	Flower	Methanolic extract	<i>B. subtilis</i>	64 µg µg/ml	36
19	Fruit	n-hexane extract	<i>B. subtilis</i>	64 µg µg/ml	36
20	Branches	n-hexane extract	<i>B. subtilis</i>	64 µg µg/ml	36

Table 4. Antifungal activity of activity of different parts of *P. mahaleb* extracted in different solvents.

S.No.	Parts used	Type of extract	Fungi inhibited	Minimum inhibitory concentration	References
1	Flower, leaves, seed kernels, fleshy seed coats, fruit stalks, branches, and resins	Methanolic extract & n-hexane extracts	<i>C. albicans</i>	16-32 µg µg/ml	36
2	Flower, leaves, seed kernels, fleshy seed coats, fruit stalks, branches, and resins	Methanolic extract & n-hexane extracts	<i>C. parapsilosis</i>	32 µg µg/ml	36
3	Leaves, seed kernels, fleshy seed coats, fruit stalks, branches, and resins	Methanolic extract & n-hexane extracts	<i>C. tropicalis</i>	32 µg µg/ml	36
4	Flower	Methanolic extract	<i>C. tropicalis</i>	64 µg µg/ml	36
5	Flower, leaves, seed kernels, fleshy seed coats, fruit stalks, branches, and resins	Methanolic extract and n-hexane extracts	<i>C. krusei</i>	64 µg µg/ml	36

Neuroprotective activity

The neuroprotective efficacy of the aqueous extract derived from *P. mahaleb* was assessed by employing hypothalamic HypoE22 cells. The MTT viability test revealed that the aqueous extract of *P. mahaleb* can enhance cell viability by over 70% when administered at concentrations ranging from 100 to 1000 µg/ml. In addition, when cells were subjected to a pro-oxidant stimulus of hydrogen peroxide at a concentration of 300 µM, the extract successfully prevented the degradation of dopamine, as indicated by the DOPAC/DA ratio (30). The main reason for the neuroprotective effect of *P. mahaleb* is the strong interaction between chicoric acid and monoamines oxidase-B (MAO-B) enzyme, which leads to improved survival of neuronal cells and subsequently reduced memory impairment. This finding has been shown by animal models of neuroinflammation (40). Moreover, another study demonstrated that the potential micromolar affinity of chicoric acid towards MAO-B caused enhancement in the neuroprotective prosperity and anti-neuroinflammatory actions exerted by other species of *P. mahaleb* (41). Additionally, it underscores the ability of chicoric acid in isolation to increase the viability of neuronal cells and decrease memory decline in diverse experimental models utilized in the induction of neuroinflammation (42). An experimental trial has been done to explore the analgesic properties of *P. mahaleb* water extract when administered orally at 12 and 24 mg/kg doses. This suggests that it could be a novel option for management of pain (5).

Anti-viral activity

Two studies have examined the antiviral efficacy of the aqueous extract of *P. mahaleb*. The first one was against the COVID-19 virus (30). The second study concluded that the aqueous extract possesses the capacity to inhibit the gene expression of two proteins, mainly angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2), which play an important role in facilitating the entry of SARS-CoV-2 into the human host (43).

Antioxidants activity

Antioxidants are substances that aid the body in protecting itself against oxidative stress, which occurs when there is an imbalance between the body's antioxidants and free radicals (44). Free radicals are extremely reactive substances that can harm cells and have a role in the development of certain chronic illnesses, such as cancer, heart disease, and neurological disorders (45-47). The seeds and fruits of *P. mahaleb* contain bioactive components, including flavonoid and phenolic compounds, which possess antioxidant activity (3,10). These chemicals can reduce oxidative stress and its harmful consequences by removing and counteracting free radicals (30). *Prunus mahaleb* extract has been the subject of several studies that have investigated their antioxidant effects using various in-vitro approaches, as indicated by literature analysis. The results of this research are summarized in Table 5. The ferric reducing antioxidant power (FRAP) and 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) assay are frequently used in-vitro techniques to assess the antioxidant properties of extracts.

Table 5. The total antioxidant capacity of the extract from the stem, bark, and fruit of *P. mahaleb* was measured by different techniques.

Part of the plant	Extract's type	Antioxidant techniques	Antioxidant capacity	References
Stem bark	Methanolic extract	2,2-diphenyl-1-picrylhydrazyl radical (DPPH)	80.9%	30
Stem bark	Methanolic extract	Reducing power assay (RPA)	89.30%	30
Seed	Methanolic extract	DPPH	44.3 %	48
Seed	Hexane extract	DPPH	26.8 %	48
Seed	Methanolic extract	Ferric reducing antioxidant power	51.P9 %	48
Seed	Hexane extract	Ferric reducing antioxidant power	32.8 %	48
Fruit	Ethanollic extract	Oxygen Radical Absorbance Capacity (ORAC)	450.550 ± 18.447 µmol /mL	3
Fruit	Ethanollic extract	Folin-Ciocalteu reducing capacity assay	22.734 ± 0.253 mg GAE/mL	3
Fruit	Methanolic extract	Cupric ion reducing antioxidant capacity (CUPRAC) assay	3.92 ± 0.26 mg Trolox/100g	49
Fruit	Methanolic extract	Ce(IV)-Based reducing capacity (CERAC) assay	15.64 mg Trolox/100g	49

Discussion

Prunus mahaleb is believed to have originated from the northern region of Iraq, as shown by its seeds, fruits, and other parts that are specifically utilized in traditional medicine, as a food additive (flavoring agent), and for aromatic uses. In Turkish traditional medicine, plant parts have been used as a tonic to treat several diseases. The fruits and seeds of the mahaleb tree, known for their bitter taste, have long been used as a remedy for the treatment of gastrointestinal problems and diabetes mellitus, as well as a heart tonic. The resins obtained from the external surface of wood have been utilized for the treatment of gastritis for many generations. Locally, herbal teas derived from stems, fruit stalks, leaves, and flowers have conventionally been employed to remedy colds and asthma in the winter season. The oil derived from the kernels by extraction has been employed in the production of liqueurs, varnished, and specialty wines due to its aromatic taste (50). The seed kernels have also been used for the management of diarrhea in children in Sudan, as well as for their sedative and vasodilator effects in Arabic countries (51).

Most of these applications have been verified through in vitro and in vivo investigations for biological assessment. The purpose of this research is to gather and analyze the existing literature on *P. mahaleb*, focusing on its botanical, ethnobotanical, phytochemical, and pharmacological aspects. *Prunus mahaleb* exhibited diverse pharmacological actions, as indicated by the literature survey. Nevertheless, a thorough examination and meticulous evaluation of the provided data allow us to deduce that the plant exhibited encouraging antibacterial, antifungal, antiviral, antioxidant, anti-inflammatory, and neuroprotective properties. Inflammation is intricately linked to a range of disorders, including atherosclerosis, cardiovascular disease, stroke, cancer, diabetes mellitus, osteoarthritis, asthma, migraine, periodontitis, irritable bowel syndrome, and chronic fatigue syndrome. Presently, the primary pharmacological agents employed for the treatment of chronic inflammatory disorders mostly consist of diverse nonsteroidal medications, which have the potential to induce adverse effects (52). Consequently, there has been a growing focus on creating efficient and organic sources of anti-inflammatory substances. Recent evidence has indicated that several types of wild fruits exhibit anti-inflammatory properties through diverse modes of action. Nitric oxide (NO) is a biomarker that indicates the presence of inflammation that occurs later in the process, specifically when inducible nitric oxide synthase (iNOS) is activated (53). Hence, the suppression of NO serves as an indication of potential anti-inflammatory characteristics. The study conducted by A. Oskoueian et al. examined the in vitro anti-inflammatory properties of methanol extracts derived from the seeds of *P. mahaleb*. The study showcased the seed extract's capacity to hinder the activity of inducible nitric oxide synthase (iNOS) while preserving cell viability (48). Cyclooxygenase -2 (COX-2) expression has a crucial role in promoting inflammation. Multiple investigations have verified the close association between COX-2, a significant

mediator of inflammation, and the onset and progression of diabetes mellitus and diabetic nephropathy (54). Therefore, the suppression of COX-2 serves as an indication of potential anti-inflammatory characteristics. A study examined the anti-inflammatory properties of a water extract derived from the fruit of *P. mahaleb*. In the ex vivo experimental paradigm, the extract successfully inhibited the up-regulation of gene expression of TNF α and COX-2 (29), which play a significant role in colon inflammation. This suggests the extract has anti-inflammatory actions in the colon, aligning with existing research (55). Tumor necrosis factor-alpha is a cytokine that plays a role in systemic inflammation. It can change the expression of adhesion molecules on cultured endothelial cells, namely human umbilical vein endothelial cells (HUVECs) (56). The response of cellular adhesion molecules to pathophysiological stimuli can impact the advancement of atherosclerosis by facilitating the interaction between blood cells, such as leukocytes and endothelial cells (57). Tumor necrosis factor-alpha can enhance the production of adhesion molecules, including intercellular cell adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1), and E-selectin, hence promoting inflammation (58). Flavonoids, which are polyphenolic substances found widely in plants, negatively correlate with cardiovascular disorders. They have preventative benefits against atherosclerosis (59). Anthocyanins, the primary flavonoid found in fruits and vegetables of *P. mahaleb*, are accountable for the vibrant red, blue, and purple hues observed in several plant-based items. The concentrated extract of *P. mahaleb* contains a significant amount of anthocyanins, flavonols, and coumarin (3). The fruit extract can reduce the expression of endothelial adhesion molecules (ICAM-1, VCAM-1, and E-selectin) in cultured HUVEC, which may result in an anti-inflammatory action (35). The majority of the studies utilized in vitro assays to examine the pharmacological activities of the extracts, such as antiproliferative, antiplatelet aggregation, and cytotoxicity. This approach was chosen because cell lines offer a more efficient and cost-effective means of screening for chemotherapeutic activity compared to in vivo assay systems (60). While the data obtained from in vitro experiments is restricted and cannot be relied upon to anticipate the results of in vivo testing, they do have the advantage of delivering high-throughput preliminary data in a more efficient manner (61). Additionally, in vitro research can be utilized to gather information that can help limit the focus of subsequent investigations, which may involve more extensive and time-consuming approaches that are also more costly (62). Antibiotics eliminate bacteria in many ways, including disrupting cell wall synthesis, inhibiting protein and nucleic acid synthesis, or functioning as anti-metabolites. Nevertheless, there has been a rise in resistance to antibiotics. While the degree and rate at which bacteria acquire resistance to antimicrobial medications may differ, resistance has emerged against all antimicrobial drugs. Furthermore, there has been a rise in the prevalence of documented clinical issues resulting from bacterial resistance to several antimicrobial agents.

Utilizing medicinal plants, potentially as part of the diet, presents a viable substitute for antimicrobial medications because of their safety, minimal side effects, lower cost, and efficacy against a broad spectrum of antibiotic-resistant microorganisms (63). Flavonoids are polyphenolic compounds that demonstrate antibacterial activity through various mechanisms of action. Multiple studies have shown that flavonoids can impede energy metabolism, cytoplasmic membrane function, and nucleic acid synthesis. Furthermore, studies have revealed that flavonoids can reduce the permeability of cell membranes, the ability of pathogens to cause disease, the presence of porin on cell membranes, the adherence of bacteria, and the creation of biofilms, all of which are crucial for bacterial growth and development (64-69). *Candida* species are currently the most prevalent and dangerous fungal pathogens, accountable for most invasive and non-invasive fungal illnesses. Currently, only four categories of antifungal medications (polyene macrolides, azoles, flucytosine, and echinocandins) can be used to treat systemic mycoses. Regrettably, none are optimal in terms of effectiveness, the range of fungi they can combat, or their safety. The n-Hexane and methanol extracts obtained from several parts of the mahaleb plant, including flowers, leaves, seed kernels, fleshy seed coats, fruit stalks, and branches, exhibited antifungal properties against *C. krusei*. However, they did not show any action against *C. albicans*, *C. parapsilosis*, or *C. tropicalis* (56). As of now, no research has been conducted to elucidate the antifungal properties of *P. mahaleb* extracts. Nevertheless, numerous phenolic compounds can serve as a defense mechanism against fungal attack and aflatoxin synthesis by inhibiting the α -amylase enzyme or exerting an antioxidant impact (70). The α -amylase enzyme plays a crucial role in the growth of microorganisms. Inhibiting this enzyme strengthens the idea that there is a connection between phenolic compounds and susceptibility to fungal infections. Previous research has demonstrated that the combined action of different compounds can help protect against contamination by harmful fungal species (71,72). The antioxidant qualities can inhibit the oxidative effects on the toxigenic fungi, preventing mycotoxins' development. Flavonoids are a wide-ranging collection of polyphenolic chemicals found in plants with antioxidant properties (73). The flavonoid composition of mahaleb exhibits variation across different genotypes and various regions of the mahaleb tree (74). Fruits exhibited the greatest overall flavonoid concentration compared to leaves and bark (75). Phenolic compounds exhibit antioxidant action by effectively neutralizing free radicals, by scavenging them, donating hydrogen atoms or electrons, or chelating metal cations (76).

Conclusion

The review above highlights that *Prunus mahaleb* L. is a noteworthy medicinal plant due to its diverse array of biological activities, which can be attributed to its rich composition of phytochemical components such as coumarins (coumarin, dihydrocoumarin, herniarin),

polyphenolic compounds (phenolic acids, flavonoids, and anthocyanins), glycosides, tannins, and Proanthocyanidins. Because of their effectiveness, these chemicals possess anti-inflammatory, analgesic, antibacterial, and antioxidant properties, which are utilized in conventional, pharmaceutical, and therapeutic applications. The objective of the review is to ascertain the specific active components accountable for the bioactivities of *Prunus mahaleb* L, which could stimulate advancements in medications, food products, and industrial applications.

Acknowledgements

The authors would like to thank the College of Pharmacy, University of Baghdad, and the Department of Pharmacy, Al-Rasheed University for their helpful supporters.

Authors' contributions

NMI participated in the design of the study and wrote the phytochemical study of the plants. TZA conceived of the study and participated in its design and coordination. ASM wrote the pharmacological activity and discussion part of the study review and participated in the sequence alignment and drafted the manuscript. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest : Authors do not have any conflict of interest to declare.

Ethical issues: None.

References

1. Komarov VL, Shishkin B, Yuzepchuk SV, Fedorov AA, Kostina KF, Kovalev NV, et al. Flora of the USSR-Volume X: Rosaceae - Rosoideae, Prunoideae. Keter Press, Jerusalem. 1970. <https://api.semanticscholar.org/CorpusID:86191147>.
2. Martín RA, Sergio MZ. Wild cherries invading natural grasslands: unraveling colonization history from population structure and spatial patterns. *Plant Ecology*. 2013; 214 (11):1299-1307. <https://doi.org/10.1007/s11258-013-0252-4>.
3. Gerardi C, Tommasi N, Albano C, Blando F, Rescio L, Pinthus E, et al. *Prunus mahaleb* L. fruit extracts: A novel source for natural food pigments. *European Food Research and Technology*. 2015; 241(5): 683–695. <https://doi.org/10.1007/s00217-015-2495-x>.
4. Zan S, Wang R, Zhang F, Zhang D, Meng X. Composition analysis of rootstock cherry (*Prunus mahaleb* L.), a potential source of human nutrition and dietary supplements. *European Food Research and Technology*. 2022; 248(22):1421–1435. <https://doi.org/10.1007/s00217-022-03965-5>.
5. Faehaa A , Ghada A. Taqa , Tahani AA, Amer AT. Determination of the ED50 and antinociceptive activity of mahaleb cherry (*Prunus mahaleb* L.) in mice. *Plant Archives*. 2020 ; 20 (1):2808-2811. <https://www.researchgate.net/profile/Ghada-Taqa/publication/341568058>.
6. Farag MA, Khattab AR, Shamma S, Afifi SM. Profiling of Primary Metabolites and Volatile Determinants in Mahlab Cherry (*Prunus mahaleb* L.) Seeds in the Context of Its Different Varieties and

- Roasting as Analyzed Using Chemometric Tools. *Foods*. 2021;10(4):728. <https://doi.org/10.3390/foods10040728>.
7. Mariod AA, Ibrahim RM, Ismail M, Ismail N. Antioxidant activities of phenolic rich fractions (PRFs) obtained from black mahlab (*Monechma ciliatum*) and white mahlab (*Prunus mahaleb*) seedcakes. *Food Chem*. 2010; 118(1), 120–127. <https://doi.org/10.1016/j.foodchem.2009.04.085>.
 8. Zühal BG, Iclal S, Akito N, Mustafa AY, Basaran AA. Antityrosinase and antimelanogenic effect of cinnamic acid derivatives from *Prunus mahaleb* L.: Phenolic composition, isolation, identification and inhibitory activity. *Journal of Ethnopharmacology*. 2023; 310: 116378. <https://doi.org/10.1016/j.jep.2023.116378>.
 9. Abedian M, Talebi M, Sayed-Tabatabaei BE, Ghobadi C. Chloroplast Microsatellite Diversity Among and Within *Prunus mahaleb* L. and *P. avium* L. Species. *Journal of Agriculture Science*. 2012; 4(5) , P. 191. <http://dx.doi.org/10.5539/jas.v4n5p191>.
 10. Blando F, Albano C, LiuY, Nicoletti I, Corradini D, Tommasi N, et al. Polyphenolic composition and antioxidant activity of the under-utilized *Prunus mahaleb* L. fruit. *J. Sci. Food Agric*. 2016; 96, 2641–2649. <https://doi.org/10.1002/jsfa.7381>.
 11. Karlovic K, Jeran N, Purgar D, Židovec V, Bolaric S, Vokurka A. Sustainable landscaping with *Prunus*. *Acta Horticulturae*. 2020; 11:75-84. 10.1766/ActaHortic.2020.1288.11.
 12. Popescu I, Caudullo G. *Prunus cerasifera* in Europe: distribution, habitat, usage and threats. In: San-Miguel-Ayanz, J., de Rigo, D., Caudullo, G., Houston Durrant, T., Mauri, A. (Eds.), *European Atlas of Forest Tree Species*. Publ. Off. EU, Luxembourg. 2016: e016531+.
 13. Chen X, Shen X, Jiang D. Complete chloroplast genome sequence of *Prunus mahaleb*. *Mitochondrial DNA Part B*. 2019; 4, 2204–2205. <https://doi.org/10.1080/23802359.2019.1624217>.
 14. Hrotkó K. Potentials in *Prunus mahaleb* L. for cherry rootstock breeding. *Sci. Hortic*. 2016; 205, 70–78. <https://doi.org/10.1016/j.scienta.2016.04.015>.
 15. Guest E, Townsend C. *Flora of Iraq*; Ministry of Agriculture of the Republic of Iraq: Baghdad, Iraq. 1966; 3: 49.
 16. Hussein ZN, Azeez HA, Salih T. Antioxidant Activity of the *Prunus mahaleb* Seed Oil Extracts Using n-Hexane and Petroleum Ether Solvents: *in-silico* and *in-vitro* Studies. *Appl. Sci*. 2023; 13(13): 7430. <https://doi.org/10.3390/app13137430>.
 17. Nadaf M, Amiri MS, Joharchi MR, Omidipour R, Moazezi M, Mohaddesi B, et al. Ethnobotanical Diversity of Trees and Shrubs of Iran: A Comprehensive Review. *International Journal of Plant Biology*. 2023; 14(1):120-146. <https://doi.org/10.3390/ijpb14010011>.
 18. Palasciano M, Ferrara G, Camposeo S, Laghezza L. Studies on *Prunus mahaleb* in Apulia. *Ital. J. Agron*. 2009; 4, 705–708.
 19. Ieri F, Pinelli P, Romani A. Simultaneous determination of anthocyanins, coumarins and phenolic acids in fruits, kernels and liqueur of *Prunus mahaleb* L. *Food Chem*. 2012; 135: 2157–2162. <https://doi.org/10.1016/j.foodchem.2012.07.083>.
 20. Lee CK, Park KK, Hwang, J K, Lee SK, Chung WY. The pericarp extract of *Prunus persica* attenuates chemotherapy-induced acute nephrotoxicity and hepatotoxicity in mice. *Journal of Medicinal Food*. 2008; 11(2):302–306. <https://doi.org/10.1089/jmf.2007.545>.
 21. Akbari F, Azadbakht M, Dashti A, Vahedi L, Davoodi A. Effect of *Prunus Mahaleb* L. Seed Extract on Ethylene glycol- and Ammonium Chloride-Induced Urolithiasis in BALB/c Mice. *Iran J Med Sci*. 2020; 45(2):134-139. <https://doi.org/10.30476/IJMS.2019.45774>.
 22. Dikbayır CY, Elmacı Y. Mahaleb Kernel Powder Improves Quality Characteristics of Sodium-Reduced Bread. *CJAFST*. 2023; 1(1): 52-64.
 23. Rana VS, Zarea SE, Sharma S, Rana N, Kumar V, Sharma U. Differential response of the leaf fruit ratio and girdling on the leaf nutrient concentrations, yield, and quality of nectarine. *Journal of Plant Growth Regulation*. 2023;42(4):2360-73.
 24. Asadi-Samani M, Moradi MT, Mahmoodnia L, Alaei S, Asadi-Samani F, Luther T. Traditional uses of medicinal plants to prevent and treat diabetes; an updated review of ethnobotanical studies in Iran. *J Nephropathol*. 2017; 6 (3): 118-125. <https://doi.org/10.15171/jnp.2017.20>.
 25. Nasab FK, Khosravi AR. Ethnobotanical study of medicinal plants of Sirjan in Kerman Province, Iran. *J. Ethnopharmacol*. 2014; 154 (1):190–197. <https://doi.org/10.1016/j.jep.2014.04.003>.
 26. Bahmani MP, Bahmani M, Shahsavari S, Naghdi N, Ezatpour B, Moradniani M, et al. A review of the antiparasitic medicinal plants used in ethnobotany of different regions of Iran. *Der Pharma Chem*. 2016; 8(2):134–138. <http://eprints.medilam.ac.ir/id/eprint/1395>
 27. Abdelgadir AA, Ahmed ME, Ahmed EM. Traditional Uses of Herbal Medicines in Khartoum and Gezira state (Central Sudan). *Arab. J. Med. Aromat. Plants*. 2021; 7(1):29–73. <https://doi.org/10.48347/IMIST.PRSM/ajmap-v7i1.22273>.
 28. Elif EE, Erdal Gül den G, Deniz A. Chemical composition, antifungal activity, antifungal mechanism, and interaction manner of the fatty acid of *Prunus mahaleb* L. with fluconazole. *International Journal of Environmental Health Research*. 2022; 32(10): 2337-2349. <https://doi.org/10.1080/09603123.2021.1963686>.
 29. Orlando G, Chiavaroli A, Adorisio S, Delfino DV, Brunetti L, Recinella L, et al. Unravelling the Phytochemical Composition and the Pharmacological Properties of an Optimized Extract from the Fruit from *Prunus mahaleb* L.: From Traditional Liqueur Market to the Pharmacy Shelf. *Molecules*. 2021; 26 (15):4422. <https://doi.org/10.3390/molecules26154422>.
 30. Seyedeh FT, Ahmad A, Javad A. Evaluation of Total Phenolic Content and Antioxidant Activity in Ten Selected Mahaleb (*Prunus mahaleb* L.) Genotypes . *Int J Hort Sci. Technol*. 2015; 2(2): 187-197.
 31. Sargar NA, Pareek S, Bhardwaj R, Vyas N. Bioactive Compounds of Loquat (*Eriobotrya japonica* (Thunb.) L.). In: Murthy H., Bapat V. (eds) *Bioactive Compounds in Underutilized Fruits and Nuts*. Reference Series in Phytochemistry [e-book]. Springer, Cham; 2020, p. 123- 143. https://doi.org/10.1007/978-3-030-30182-8_10.
 32. Kahif G, Isam AM, Süleyman D, Nurhan U, Gbemisola FJ, Fahad A, et al. The Effect of Heating Temperature on Total Phenolic Content, Antioxidant Activity, and Phenolic Compounds of Plum and Mahaleb Fruits. *International Journal of Food Engineering*. 2019; 15(11-12): 20170302. <https://doi.org/10.1515/ijfe-2017-0302>.
 33. Nabaa MI, Enas JK, Shihab HM. Isolation of Catchin and Epigallocatechin From Iraqi Rhus coriaria By Preparative High-Performance Liquid Chromatography (PHPLC). *Iraqi J Pharm Sci*. 2022; 31(2): 271-282. <https://doi.org/10.31351/vol31iss2pp271-282>.
 34. Maja N, Dragana DZ, Ivanka Č, Mekjell M, Biljana R, Milica FA. Chapter 56 - Cold pressed oils from genus *Prunus*, Editor(s): Mohamed Fawzy Ramadan, *Cold Pressed Oils* [e-book]. Academic Press; 2020:637-658. <https://doi.org/10.1016/B978-0-12-818188-1.00056-6>.
 35. Gerardi C, Frassinetti S, Caltavuturo L, Leone A, Lecci R, Calabriso N, et al. Anti-proliferative, anti-inflammatory, and anti-mutagenic activities of a *Prunus mahaleb* L. anthocyanin-rich

- fruit extract. *Journal of Functional Foods*. 2016; 27: 537-548. <https://doi.org/10.1016/j.jff.2016.09.024>.
36. Berrin O, Ufuk K, Durmuş K, Nazim S. Evaluation of the in vitro bioactivities of Mahaleb Cherry (*Prunus mahaleb* L. Romanian Biotechnological Letters. 2012; 17: 7863-7872.
 37. Seyyednejad SM, Maleki S, Damabi NM, Motamedi H. Antibacterial activity of *Prunus mahaleb* and Parsley (*Petroselinum crispum*) against some pathogen. *Asian J Biol Sci*. 2008; 1(1): 51-55. DOI: 10.3923/ajbs.2008.51.55
 38. Bayramcı NS, Erdönmez D, Budak Y, Eğri Ö. Antibacterial activity of ethanol extracts of mahaleb cherry (*Prunus mahaleb* L.) against some bacteria. *Current Opinion in Biotechnology*. 2013; 24(S1):113. <https://doi.org/10.1016/j.copbio.2013.05.349>.
 39. Al-Nagerabi SAF, Al-Maqbali MSR, Alabri KMS, Elshafei AE. An in Vitro Antifungal and Antiaflatoxic Properties of *Commiphora myrrha* and *Prunus mahaleb*. *Journal of Food Research*. 2021; 10 (6):10. <https://doi.org/10.5539/jfr.v10n6p10>.
 40. Liu Q, Fang J, Chen P, Die Y, Wang J, Liu Z, et al. Chicoric acid improves neuron survival against inflammation by promoting mitochondrial function and energy metabolism. *Food Funct*. 2019; 10 (9): 6157–6169. <https://doi.org/10.1039/C9FO01417A>
 41. Bonaventura MVMD, Martinelli I, Moruzzi M, Bonaventura EMD, Giusepponi ME, Polidori C, et al. Brain alterations in high fat diet induced obesity: Effects of tart cherry seeds and juice. *Nutrients*. 2020; 12 (3): 623. <https://doi.org/10.3390/nu12030623>.
 42. Liu Q, Chen Y, Shen C, Xiao Y, Wang Y, Liu, Z, et al. Chicoric acid supplementation prevents systemic inflammation-induced memory impairment and amyloidogenesis via inhibition of NF- κ B. *FASEB J*. 2017; 31 (4): 1494–1507. <https://doi.org/10.1096/fj.201601071R>.
 43. Sungnak W, Huang N, Bécavin C, Berg M, Queen R, Litvinukova M, et al. SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. *Nat. Med*. 2020; 26, 681–687. <https://doi.org/10.1038/s41591-020-0868-6>.
 44. Mititelu RR, Pădureanu R, Băcănoiu M, Pădureanu V, Docea AO, Calina D, et al. Inflammatory and Oxidative Stress Markers—Mirror Tools in *Rheumatoid Arthritis*. *Biomedicines*. 2020; 8 (5):125. <https://doi.org/10.3390/biomedicines8050125>.
 45. Salehi B, Quispe C, Chamkhi I, El Omari N, Balahbib A, Sharifi-Rad J, et al. Pharmacological properties of chalcones: a review of preclinical including molecular mechanisms and clinical evidence. *Front in Pharmacology*. 2021; 11: 592654. <https://doi.org/10.3389/fphar.2020.592654>.
 46. Salehi B, Prakash Mishra A, Nigam M, Karazhan N, Shukla I, Kieltyka-Dadasiewicz A, et al. Ficus plants: state of the art from a phytochemical, pharmacological, and toxicological perspective. *Phytotherapy Res*. 2021; 35 (3):1187–1217. <https://doi.org/10.1002/ptr.6884>.
 47. Salehi B, Sharifi-Rad J, Cappellini F, Reiner Ž, Zorzan D, Imran M, et al. The therapeutic potential of anthocyanins: current approaches based on their molecular mechanism of action. *Frontiers in Pharmacology*. 2020 (11): 1300. <https://doi.org/10.3389/fphar.2020.01300>.
 48. Oskoueian A, Haghghi RS, Ebrahimi M, Saad WZ, Omar AR, Ho YW. Bioactive compounds, antioxidants, tyrosinase inhibition, xanthine oxidase inhibition, anticholinesterase and antiinflammatory activities of *Prunus mahaleb* L. Seed. *J. Med. Plants Res*. 2012;6(2): 225–233. <https://doi.org/10.3390/ijms12128610>.
 49. Gerçek YC, Ozyurt D, Erol O, Ozturk BD, OZ GC, et al. Comparison of polyphenolic profile and antioxidant capacity of *Prunus subgenus cerasus* L. species from Turkey. *Eur Food Res Technol* 249, 1363–1376 (2023). <https://doi.org/10.1007/s00217-023-04219-8>.
 50. Özçelik B, Koca U, Kaya DA, Şekerolu N. Evaluation of the in vitro bioactivities of mahaleb cherry (*Prunus mahaleb* L.). *Rom. Biotechnol Lett*. 2012; 17(6): 7863–7872.
 51. Güven ZB, Alshehri O, Yüce N, Bakan E, Demirci B, Yılmaz MA, et al. Chemical composition, nutritional values, elemental analysis and biological properties of *Prunus mahaleb* L.: From waste to new potential sources for food, cosmetic and drug industry. *Food Bioscience*. 2023; 53: 102632. <https://doi.org/10.1016/j.fbio.2023.102632>.
 52. Cuevas-Rodriguez EO, Dia VP, Yousef GG, Garcia-Saucedo PA, Lopez-Medina J, Paredes-Lopez O, et al. Inhibition of pro-inflammatory responses and antioxidant capacity of Mexican blackberry (*Rubus* spp.) extracts. *J Agric Food Chem*. 2010; 58:9542–9548. <https://doi.org/10.1021/jf102590p>.
 53. Stamler JS, Single D, Loscalzo J. Biochemistry of nitric oxide and its redox-activated forms. *Science*. 1992; 258: 1892–1902. <https://doi.org/10.1126/science.1281928>.
 54. Li Y, Zhang J.-J, Xu D.-P, Zhou T, Zhou Y, Li S, et al. Bioactivities and Health Benefits of Wild Fruits. *Int J Mol Sci*. 2016; 17: 1258. <https://doi.org/10.3390/ijms17081258>.
 55. Ferramosca A, Treppiccione L, Di Giacomo M, Aufiero VR, Mazzarella G, Maurano F, et al. *Prunus Mahaleb* Fruit Extract Prevents Chemically Induced Colitis and Enhances Mitochondrial Oxidative Metabolism via the Activation of the Nrf2 Pathway. *Mol. Nutr. Food Res*. 2019; 63: 1900350. <https://doi.org/10.1002/mnfr.201900350>
 56. Lu ZY, Chen WC, Li YH, Li L, Zhang H, Pang Y, Xiao ZF, Xiao HW, Xiao Y. TNF- α enhances vascular cell adhesion molecule-1 expression in human bone marrow mesenchymal stem cells via the NF- κ B, ERK and JNK signaling pathways. *Mol Med Rep*. 2016;14(1):643-8. <https://doi.org/10.3892/mmr.2016.5314>. Epub 2016 May 19.
 57. Schumski A, Winter C, Döring Y, et al. The ins and outs of myeloid cells in atherosclerosis. *J Innate Immun* 2018;10:479–86. <https://doi.org/10.1159/000488091>.
 58. Jia Z, Nallasamy P, Liu D, Shah H, Li JZ, Chitrakar R, et al. Luteolin protects against vascular inflammation in mice and TNF-alpha-induced monocyte adhesion to endothelial cells via suppressing IKK α /NF- κ B signaling pathway. *J Nutr Biochem*. 2015; 26(3):293-302. <https://doi.org/10.1016/j.jnutbio.2014.11.008>
 59. Chen T, Zhang X, Zhu G, Liu H, Chen J, Wang Y, He X. Quercetin inhibits TNF- α induced HUVECs apoptosis and inflammation via downregulating NF- κ B and AP-1 signaling pathway in vitro. *Medicine (Baltimore)*. 2020; 99 (38):e22241. <https://doi.org/10.1097/MD.00000000000022241>.
 60. Chang BK. Comparison of in vitro methods for assessing cytotoxic activity against two pancreatic adenocarcinoma cell lines. *Cancer Research*. 1983; 43(7): 3147–3149.
 61. Blumenthal RD, Goldenberg DM. Methods and goals for the use of in vitro and in vivo chemo-sensitivity testing. *Molecular Biotechnology*. 2007; 35(2): 185–197. <https://doi.org/10.1007/BF02686104>
 62. Yang Y, Balcarcel RR. 24-well plate spectrophotometric assay for preliminary screening of metabolic activity. *Assay Drug Dev Technol*. 2003; 1(3):461-8. <https://doi.org/10.1089/154065803322163777>.
 63. Lin RD, Chin YP, Lee MH. Antimicrobial activity of antibiotics in combination with natural flavonoids against clinical extended-spectrum beta-lactamase (ESBL)-producing *Klebsiella pneumoniae*. *Phytother Res*. 2005; 19(7):612-7. <https://doi.org/10.1002/ptr.1695>.

64. Xie Y., Yang W., Tang F., Chen X., Ren L. Antibacterial Activities of Flavonoids: Structure-Activity Relationship and Mechanism. *Curr. Med. Chem.* 2014; 22:132–149. <https://doi.org/10.2174/0929867321666140916113443>.
65. Cushnie TP, Lamb AJ. Antimicrobial activity of flavonoids. *Int J Antimicrob Agents.* 2005; 26(5):343-56. <https://doi.org/10.1016/j.ijantimicag.2005.09.002>.
66. Górnica I, Bartoszewski R, Króliczewski J. Comprehensive review of antimicrobial activities of plant flavonoids. *Phytochem. Rev.* 2019;18:241–272. <https://doi.org/10.1007/s11101-018-9591-z>.
67. Biharee A, Sharma A, Kumar A, Jaitak V. Fitoterapia Antimicrobial flavonoids as a potential substitute for overcoming antimicrobial resistance. *Fitoterapia.* 2020;146:104720. <https://doi.org/10.1016/j.fitote.2020.104720>.
68. Wu T, Zang X, He M, Pan S, Xu X. Structure–Activity Relationship of Flavonoids on Their Anti-*Escherichia coli* Activity and Inhibition of DNA Gyrase. *J. Agric. Food Chem.* 2013;61:8185–8190. <https://doi.org/10.1021/jf402222v>.
69. Donadio G, Mensitieri F, Santoro V, Parisi V, Bellone M, De Tommasi N, et al. Interactions with Microbial Proteins Driving the Antibacterial Activity of Flavonoids. *Pharmaceutics.* 2021;13:660. <https://doi.org/10.3390/pharmaceutics13050660>.
70. Silva B, Souza MM, Badiale-Furlong E, Manuel M. Souza, and Eliana Badiale-Furlong. "Antioxidant and antifungal activity of phenolic compounds and their relation to aflatoxin B1 occurrence in soybeans (*Glycine max* L.). *Journal of the Science of Food and Agriculture.* 2020, 100: 1256-1264. <https://doi.org/10.1002/jsfa.10137>.
71. Telles AC, Kupski L, Furlong EB. Phenolic compound in beans as protection against mycotoxins. *Food Chemistry.* 2017; 214:293–299. <https://doi.org/10.1016/j.foodchem.2016.07.079>
72. Pagnussatt FA, Rodrigues V, Dora CL, Costa JAV, Putaux JL, Badiale Furlong E. Assessment of the encapsulation effect of phenolic compounds from *Spirulina sp.* LEB-18 on their antifusarium activities. *Food Chemistry.* 2016; 211:616–623. <https://doi.org/10.1016/j.foodchem.2016.05.098>
73. Tanaka Y, Sasaki N, Ohmiya A. Biosynthesis of Plant Pigments: Anthocyanins, Betalains and Carotenoids. *Plant J.* 2008; 54 (4): 733-749. <https://doi.org/10.1111/j.1365-313X.2008.03447.x>.
74. Taghizadeh SF, Asgharzadeh A, Asili J, Sahebkar A, Shakeri A. Evaluation of Total Phenolic Content and Antioxidant Activity in Ten Selected Mahaleb (*Prunus mahaleb* L.) Genotypes. *Int. J. Hortic. Sci. Technol.* 2015; 2 (2): 187-97. <https://doi.org/10.22059/ijhst.2015.56435>.
75. Pehlivan FE. Antioxidant and phenolic profile of mahaleb plant as a functional food. *J Agric Sci Technol.* 2021; B 11: 46-51. <https://doi.org/10.17265/2161-6264/2021.01.004>
76. Medini F, Fellah H, Ksouri R, Abdely C. Total Phenolic, Flavonoid and Tannin Contents and Antioxidant and Antimicrobial Activities of Organic Extracts of Shoots of the Plant *Limonium delicatulum*. *J. Taibah Univ. Sci.* 2014; 8 (3): 216-24. <https://doi.org/10.1016/j.jtusci.2014.01.003>.