

Nutraceutical potential of parsley (Petroselinum crispum Mill.): Comprehensive overview

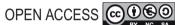
Waheeba E. Ahmed^{1,2}, Albandari A. Almutairi¹, Mona S. Almujaydil¹, Raya Algonaiman¹, Hassan Mirghani Mousa¹, Raghad M. Alhomaid^{1°}

¹Department of Food Science and Human Nutrition, College of Agriculture and Food, Qassim University, Buraydah, Saudi Arabia; ²Department of Food Science and Technology, Alzaiem Alazhari University, Sudan

*Corresponding Author: Raghad M. Alhomaid, Department of Food Science and Human Nutrition, College of Agriculture and Food, Qassim University, Buraydah 51452, Saudi Arabia. Email: r.alhomaid@qu.edu.sa

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REVIEW ARTICLE

Abstract

Leafy vegetables are widely recognized for their significant contribution to human health. Among them, parsley (Petroselinum crispum Mill.) is a promising herb with considerable potential to facilitate various favorable effects on health. This review provides a comprehensive overview of the health effects of parsley, highlighting its potential in promoting several health benefits. The available studies suggest that parsley possesses antioxidant and anti-inflammatory properties, exhibits potential for diabetes management, demonstrates hepatoprotective and nephroprotective effects, and shows promise in terms of its potential anticancer properties, among other health-promoting effects. These beneficial effects are attributed to the presence of bioactive compounds in parsley, including phenolic acids and flavonoids, which contribute to its antioxidant capacity. Furthermore, parsley contains key bioactive substances, such as myricetin and apiol, which significantly contribute to its health-promoting properties. In addition, parsley is a rich source of essential vitamins and minerals, making it a valuable herb and a substantial reservoir of nutrients. In conclusion, incorporating parsley into daily diet can enhance overall well-being. Considering the individual variations in potential health benefits, it is crucial to seek guidance from healthcare professionals or nutritionists. This ensures a personalized and evidence-based approach to sustainably integrate parsley into individuals' daily diets.

Keywords: antioxidantes, plants, pasrsley, nutrition, public health, obesity

Introduction

For decades, the significant impact of consuming nutritious food sources has been well documented. Providing a sustainable diet rich in nutritive substances, such as dietary fibers, vitamins, minerals, and other essential components, undoubtedly contributes to the improvement of human well-being. Nutritious foods play a crucial role in supporting optimal physical and mental health, promoting growth and development, and reducing the risk of chronic diseases (Chen *et al.*, 2018; Townsend *et al.*, 2023). Studies have linked the progression and development of

chronic diseases to an inadequate diet. Chronic diseases, such as cardiovascular diseases, type 2 diabetes, obesity, certain types of cancers, and neurodegenerative disorders, have complex etiologies influenced by multiple factors, including genetics and lifestyle and dietary choices. An inadequate diet lacking essential nutrients with excessive unhealthy components (such as saturated and trans fats, added sugars, and sodium) or low in dietary fibers, vitamins, minerals, and bioactive compounds can contribute to the development and progression of chronic diseases (Ali *et al.*, 2020; Gropper, 2023; Rappaport, 2016; Steyn and Damasceno, 2006; Teodoro, 2019). Moreover,

consumption of specific nutrients, known as nutraceuticals, can have a substantial impact on human health and further improve overall well-being. Nutraceuticals are bioactive compounds or substances derived from food sources that provide health benefits beyond basic nutrition (Al Ali *et al.*, 2021; Nasri *et al.*, 2014).

Green leafy vegetables, such as parsley (Petroselinum crispum Mill.), have been acknowledged widely for their significant contribution to human health because of their abundant supply of essential nutrients and bioactive compounds, classified as nutraceuticals. Parsley, a resourceful herb cultivated and consumed for centuries, has a long and fascinating history originating from the Mediterranean and Middle East regions, particularly in Italy, Greece, and Lebanon. It is valued for its distinct flavor and aromatic qualities and is used in both culinary and traditional medicines. Since ancient times, parsley is believed to have diuretic properties and has been used as a traditional remedy for kidney stones. Ancient cultures utilized parsley to address health issues, such as menstrual disorders, gastritis, and prostatitis (Agyare et al., 2017; Charles, 2012; Kumar et al., 2016). Its historical uses have attracted the attention of researchers, leading to investigations of the health claims associated with the herb. Numerous studies have discovered beneficial effects of consuming parsley for various health conditions, such as preventing liver and kidney damage (Ashry et al., 2021; Bastampoor et al., 2021; Goda et al., 2023), enhancing cognitive functions (Ertik et al., 2023; Sener et al., 2022), and alleviating metabolic disorders (Eshak and Mahran, 2018; Soliman et al., 2015). Parsley has a dense nutritional composition with various bioactive components. It is rich in vitamins and minerals, including vitamins A and K, ascorbic acid, potassium, iron, and zinc. Additionally, it contains a wide range of bioactive substances, such as phenylpropenes, phenolics, and pigments (Farouk et al., 2017; US Department of Agriculture, 2019; Zhang et al., 2006). This diverse profile of parsley suggests that it has a strong potential to promote various health benefits. This review aimed to provide a comprehensive overview of the health benefits of parsley, highlighting its potential in promoting various favorable outcomes. By synthesizing the existing studies and research findings, our objective was to reveal the potential health benefits associated with parsley consumption and to present a holistic understanding of its impact on human well-being.

Botanical Description and Longevity Attributes

Parsley (*Petroselinum crispum* Mill.) is a vibrant green herb characterized by distinctive aroma and flavor. It belongs to the Apiaceae family, commonly known as the carrot or parsley family. The scientific name of parsley, *Petroselinum*, has its roots in the Greek words *petros*, meaning 'stone' (indicating its ability to thrive in rocky environments), and *selinon*, referring to 'celery'. Throughout the Middle Ages, the name underwent transformations, evolving from petrocilium to petersylinge, persele, persley, and eventually settling on the familiar term 'parsley', presently recognized in English (Charles, 2004; Daradkeh and Essa, 2016).

Parsley is a biennial herbaceous plant grown in sunny areas with suitable environmental conditions, favorably in humid soil with a pH ranging from 5.3 to 7.3. In such conditions, it could grow up to a height of 60-120 cm but typically reaches 20-30 cm. It is sensitive to water stress, especially if it is planted in the summer and at the end of spring, thereby providing a permanent source of water that can increase its production and improve growth quality. Morphologically, parsley forms a dense, bushy clump with upright, ribbed, and branched stems. Its compound leaves consist of bright green, glossy leaflets with smooth or slightly toothed margins. The leaflets are ovate to triangular in shape and arranged in a pinnate or bipinnate fashion (Figure 1). The seeds are round or pear-like in shape, with a strong lateral compression. They range in color from greenish gray to grayish brown and consist of two connected achenes. These achenes can easily be separated along the commissural surface, revealing mericarps that resemble a sickle shape. The mericarps measure up to 2 mm in length and 1-2 mm in width (Figure 2) (Agyare et al., 2017; Charles, 2012).

Parsley's longevity during storage is influenced by various factors, including temperature, humidity, and proper trimming of stems, all of which contribute to preserving its freshness. Refrigeration is commonly employed and can extend the storage capacity of fresh parsley to approximately 1-2 weeks. However, longer storage durations can be achieved under specific conditions. When stored at a temperature of 0°C, parsley can maintain its quality for up to 1-2 months, while in a cold store at 0-2°C, it can remain fresh for over 12 days. These lower temperatures help to slow down the degradation processes and preserve parsley's vibrant appearance and flavor (Cătunescu et al., 2012; Daradkeh and Essa, 2016). It is worth noting that other factors, such as air circulation, packaging methods, and initial quality of parsley, can impact its shelf life. Exploring alternative preservation techniques, such as drying, can further extend the storage duration of parsley (Dziki et al., 2022).

Nutritional Composition and Bioactive Content

Parsley is a nutrient-rich herb with a distinct nutritional composition, characterized by moderate amounts of



Figure 1. Leaves of parsley (Petroselinum crispum).



Figure 2. (A) Seeds, (B) roots, and (C) flowers of parsley (Petroselinum crispum).

dietary fiber and rich amounts of vitamins and minerals, along with a diverse array of bioactive phytonutrients, such as phenolic acids and flavonoids; the latter representing its unique nutritional composition. This section discusses both minor and major nutritional characteristics of parsley leaves.

Parsley provides an intense nutrient profile with a low-calorie intake; almost each 100 g of fresh parsley contains 36 calories. In addition to this low-calorie intake, approximately 3 g of dietary fiber can be obtained per 100 g of parsley, which nearly provides 10.7% of the average dietary reference intake (DRI) of fiber (National Institutes of Health [NIH], n.d.; US

Department of Agriculture, 2019). Carbohydrates and protein are also present in parsley but in relatively minimal quantity. However, the macronutrient content of parsley is significantly lower compared to its abundance of vitamins and minerals (Table 1). Vitamins and minerals are universally recognized as essential nutrients for various physiological functions of human body, including immune support, energy production, and sustaining optimal bone and muscle health. Diversifying the intake of vitamin- and mineral-rich foods is advisable to meet daily nutritional requirements to enhance the overall well-being (Gharibzahedi and Jafari, 2017; Maqbool *et al.*, 2017). Parsley's has an excellent diversity of vitamins, including vitamins C, A, E (mainly α-tocopherol),

K (phylloquinone), and B-complex. As shown in Table 1, this wide range of vitamins can almost provide per 100 g of fresh parsley leaves an average range of 5–38% of DRI for both adult males and females, with vitamins C and K providing nearly an average of more than 150% DRI. Selected minerals, such as potassium, calcium, and zinc, found in fresh parsley leaves also provide 7–17% of DRI to both adult males and females (NIH, n.d.).

Furthermore, parsley leaves not only provide essential vitamins and minerals but they are also a rich source of a diverse array of phytonutrients, such as phenylpropenes, phenolics, and pigments (Table 2). These constituents potentially function as nutraceuticals by augmenting the nutritional value and health-enhancing properties of

parsley. Phenylpropenes, for instance, potentially exhibit biological activities along with their contribution to the distinct flavors and aromas of plants. Phenylpropenes are mainly found in the plant's essential oils, which are responsible for their characteristic fragrances (Burčul et al., 2020). The main phenylpropenes that dominate parsley essential oils are myristicin and apiol, comprising 32.75% and 17.54% of its total chemical composition, respectively (Zhang et al., 2006). Phenolic compounds, on the other hand, contribute to both flavor and color of plants along with playing a key role in plant physiology and defense mechanisms. Phenolic compounds are well demonstrated to exhibit health-promoting properties, such as antimicrobial, anti-inflammatory, and antioxidant effects (Kumar and Goel, 2019; Ullah et al., 2020). Parsley

Table 1. Nutritional composition of parsley leaves (Petroselinum crispum).

Component	Dry leaves	Fresh leaves	DRI (%)*
Macronutrients (g 100 g ⁻¹)			
Fat		$0.79^{(2,6)}$	
Protein		2.97(4); 3.10(2)	
Carbohydrates		5.33 ⁽²⁾ ; 6.33 ⁽⁴⁾	
Dietary fiber		3.3 ⁽⁴⁾ ; 4 ⁽²⁾	12.10
Energy (Kcal 100 g ⁻¹)		36(4)	
Vitamins			
Vitamin A (μg 100 g ⁻¹)		400(2); 421(4)	51
Vitamin C (mg 100 g ⁻¹)	248.31 ⁽¹⁾ ; 138-163 ⁽³⁾	125 ⁽²⁾ ; 133 ⁽⁴⁾	156.4
Vitamin E (mg 100 g ⁻¹)		0.60(2)	5.6
α -tocopherol		$0.75^{(4)}$	
γ-tocopherol		$0.53^{(4)}$	
Vitamin K (μg 100 g ⁻¹)		164 ⁽⁴⁾	156
B complex (mg 100 g ⁻¹)			
Thiamine		0.086(4)	7.49
Riboflavin		0.098(4)	8.22
Niacin		1.31(4)	8.77
Pantothenic acid		0.4(4)	8
Pyridoxine		$0.09^{(4)}$	6.92
Folate (µg 100 g ⁻¹)		152 ⁽⁴⁾	38
Minerals (mg 100 g ⁻¹)			
Potassium		450 ⁽²⁾ ; 554 ⁽⁴⁾	17
Calcium		120(2); 138(4)	13
Magnesium		50(4)	14
Manganese		0.14(2); 0.16(4)	
Sodium		53 ⁽²⁾ ; 56 ⁽⁴⁾	
Phosphorus		42.65(2); 58(4)	7.19
Iron		5.55 ⁽²⁾ ; 6.2 ⁽⁴⁾	53
Zinc		$0.99^{(2)}$; $1.07^{(4)}$	11
Copper		0.149(4)	16.56

⁽¹)Kuźma et al., 2014; (²)Eshak and Mahran, 2018; (³)Karklelienė et al., 2014; (⁴)US Department of Agriculture, 2019; (⁵)Justesen and Knuthsen, 2001. *Calculated as an average daily reference intake (DRI) for both adult males and females, based on the mean values of estimated components.

Table 2. Main phytonutrients found in parsley (Petroselinum crispum).

Component	Dry leaves	Fresh leaves
Phenylpropenes (%)*		
Myristicin		32.75(9); 26.21(10)
Apiol		17.54 ⁽⁹⁾
β-Phellandrene		11.61(10)
lpha-Phellandrene		10.54 ⁽¹⁰⁾
p-Cymenene		8.63(10)
Phenolics		
Total (mg GAE 100 g ⁻¹)	920 ⁽⁴⁾ ; 700 ⁽⁶⁾	985 ⁽⁵⁾ ; 1,740 ⁽⁶⁾
Phenolic acids (mg 100 g ⁻¹)		
Caffeic acid	85.67 ⁽⁸⁾	
Ferulic acid	27.07 ⁽⁸⁾	
Chlorogenic acid	171.30 ⁽⁸⁾	
Cinnamic acid		
Protocatechuic acid		
Gallic acid	37.49(8)	
Syringic acid	9.49(8)	
Vanillic Acid	26.31(8)	
Flavonoids (mg 100 g ⁻¹)		
Total (mg QE 100 g ⁻¹)	1,435 ⁽⁷⁾	
Catechin	5.36-13.82 ⁽¹⁾	
Apigenin	510-630 ⁽³⁾ ; 1,316 ⁽⁶⁾	1,375.2 ⁽⁶⁾
Kaempferol		
Luteolin	24.17(8)	
Cynaroside		
Rutin	22.03(8)	
Chrysoeriol		
Apiin		
Quercetin	19.89 ⁽⁸⁾	
Pigments		
Carotenoids (mg 100 g ⁻¹)	31.28 ⁽¹⁾ ; 2–16 ⁽²⁾	
Chlorophyll (mg g ⁻¹)	0.185 ⁽¹⁾ ; 0.09-0.87 ⁽²⁾	

⁽¹)Kuźma et al., 2014; (²)Dobričević et al., 2019; (³)Justesen and Knuthsen, 2001; (4)Farah et al., 2015; (5)Slimestad et al., 2020; (6)Henning et al., 2011; (7)Chandra et al., 2014; (8)Derouich et al., 2020; (9)Zhang et al., 2006; (10)Farouk et al., 2017.

is known to contain rich amounts of phenolic compounds with total content ranging from 700 to 920 mg of gallic acid equivalent (GAE) per 100 g of its dried leaves. Fresh parsley leaves may have a total of 1,740 mg GAE per 100 g of phenolic compounds (Farah *et al.*, 2015; Henning *et al.*, 2011). Parsley's phenolics, phenolic acids, and flavonoids contribute to its distinct flavor while providing additional health-promoting effects. Caffeic acid, ferulic acid, syringic acid, and chlorogenic acid are among the various phenolic acids found in parsley, with amounts ranging from 9 to 171 mg per 100 g of dried parsley leaves. Among parsley's flavonoids are quercetin, rutin, luteolin, and apigenin,

with their quantities ranging from 19 to 630 mg per 100 g of dried parsley leaves (Derouich *et al.*, 2020; Justesen and Knuthsen, 2001). Other major constituents that contribute to the color of parsley are its pigments, primarily chlorophyll and carotenoids. Chlorophyll is responsible for the green color of parsley, while carotenoids contribute to its yellow to orange hues. Parsley contains chlorophyll and carotenoids in the range of 0.09–0.87 mg per g and 2–31 mg per 100 g of dried leaves, respectively. These pigments not only provide visual appeal to parsley but also play a vital role in the process of photosynthesis, especially chlorophyll. In addition to offering health benefits to both

^{*}Estimated in parsley essential oil.

GAE: gallic acid equivalent; QE: quercetin acid equivalent.

plants and humans, carotenoids, in particular, play the role of radical scavenger that protects the plant from oxidative damage. It also provides antioxidant activity to the body along with offering other potential health benefits, such as anti-inflammatory and anticancer effects (Chandra *et al.*, 2014; Dobričević *et al.*, 2019; Kuźma *et al.*, 2014).

Traditional Applications and Cultural Significance

Parsley for long has played a significant role in culinary traditions, cultural practices, and traditional medicines around the world. Renowned for its fresh and vibrant flavor profile, this unassuming herb, characterized by delicate leaves and a distinctive aroma, for long has been revered for its ability to impart a burst of freshness to various dishes. Beyond its culinary attributes, parsley holds profound cultural significance, finding a place in diverse traditions and celebrations. This section discusses the versatile uses of parsley in global cuisines, examining its culinary appeal and the intricate cultural symbolism it carries. Furthermore, the lesser-known applications of parsley in traditional medicines across different cultures are discussed, shedding light on its potential health benefits and therapeutic properties.

Culinary applications and cultural significance

Parsley leaves are extensively utilized in culinary practices and have a cultural importance in diverse cuisines globally. It is commonly employed as a decorative element for adding vibrant color and a touch of freshness to numerous dishes, such as soups, stews, salads, and sauces. Parsley is also used as an ingredient in cooked meals to enhance flavors and provide nutritional benefits. The native homeland of parsley is the Mediterranean and Middle East regions, specifically in the eastern Mediterranean and western Asia (Charles, 2004, 2012; Kumar et al., 2016; Odobasic et al., 2017). In western Asian regions, such as Lebanon, Palestine, and Turkey, parsley is commonly used in traditional cuisines, such as tabbouleh, a popular Middle Eastern salad that prominently features a high portion of finely chopped parsley along with bulgur wheat, tomatoes, onions, and a dressing of lemon juice and olive oil. Parsley serves as the foundation of this refreshing and nourishing salad, contributing to its vibrant green color and a distinctively fresh and intense flavor. In addition to tabbouleh, parsley is widely used as a key ingredient in numerous other Middle Eastern cuisines. For instance, Iraqi cuisine commonly utilizes parsley as a key ingredient in the stuffing mixture of various vegetables, providing a delightful flavor and a refreshing touch to common dishes such as stuffed grape leaves 'dolma', stuffed bell peppers, and stuffed zucchini (Al-Khusaibi, 2019; Nasrallah, 2009). Another notable use of parsley is found in the widely enjoyed dish called *mujaddara*, a native comforting Palestinian cuisine that features a delightful combination of lentils, rice, and caramelized onions. Parsley is often incorporated as a garnish, serving to elevate flavors and introduce a refreshing element to the overall composition of the dish (Khan, 2018). The exploration of parsley's applications in these regions is by no means exhaustive, as its utilization extends to a wide array of dishes. This expansive usage serves to highlight the remarkable versatility and noteworthy significance of parsley within the esteemed gastronomic Mediterranean and Middle Eastern cultures.

Beyond Mediterranean and Middle Eastern regions, the utilization of parsley has expanded since the 16th century, with discovering its route into the culinary traditions of many other countries, including certain European cultures. In French cuisine, parsley is a key ingredient for creating *bouquet garni*, a herb bundle used for enhancing the flavors of stocks, stews, and sauces. Parsley is frequently used as an important component in certain French dishes, such as *moules marinières*, a popular dish featuring cooked mussels prepared with white wine, shallots, butter, and parsley (Julien-David and Marcic, 2020).

Apart from parsley's culinary applications, it is believed to have a cultural and symbolic significance in certain European folklore and traditions. In ancient Greek and Roman cultures, parsley was not commonly cultivated for consumption but rather for other high values. Greek folklore often incorporated parsley as a key feature in festive celebrations, and it was frequently used as a decorative element during Easter festivities. Moreover, parsley seeds are associated with superstitions, with beliefs that they possess extraordinary ability to repel evil spirits. In Roman culture, parsley served as a means to counteract garlic odor. Furthermore, in both Greek and Roman cultures, parsley was considered an exceptional fodder for their chariot horses, with the belief that it provided exceptional nourishment and strength to the animals (Agyare et al., 2017; Charles, 2012).

Parsley as a traditional medicine

Parsley has a long history of being used in various traditional medicinal practices across different cultures. One of the most common medicinal uses of parsley is to manage urinary tract infection and fluid retention. It is often employed as a diuretic agent for treating kidney stones. Additionally, in traditional Turkish and some other cultures, parsley is utilized for managing bleeding, hypertension, hyperlipidemia, hepatic disorders, and diabetes.

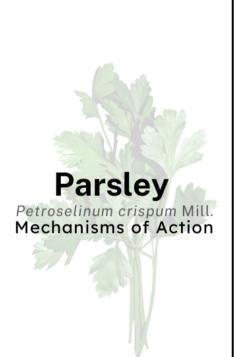
In several European countries, such as Spain, Italy, and Serbia, parsley is used to treat a wide range of ailments, such as lumbago, eczema, nosebleeds, menstrual disorders, gastritis, prostatitis, constipation, anemia, toothache, halitosis, baldness, and even for inducing abortion. In regions such as Iraq and Morocco, parsley leaves are applied to treat skin disorders, arterial and cardiac diseases, lumbago, eczema, and nosebleeds (Agyare *et al.*, 2017; Charles, 2012). In traditional Chinese medicine, parsley is significantly employed to tonify and enrich the blood, regulate the body's water balance, and help eliminate toxins. It is believed to have positive effects on digestion and promote a sense of well-being. In India, parsley is utilized for treating cold, cough, fever, stomach issues, and indigestion (Charles, 2012; Punoševac *et al.*, 2021).

Nutraceutical Potential and Health-Promoting Effects

As discussed in the previous section, parsley leaves exhibit a remarkable profile of nutritional and bioactive constituents. The presence of bioactive constituents indicates substantial potential in the management and prevention of various health conditions (Figure 3). This section highlights the predominant health-enhancing effects attributed to the consumption of parsley.

Antioxidant effects

Parsley's abundant contents of phenolic compounds and other bioactive components, such as carotenoids, can boost its radical scavenging activity. Free radicals, or reactive oxygen species (ROS), are highly reactive molecules that if produced in amounts exceeding the body's antioxidant defenses can cause oxidative damage, the phenomenon known as oxidative stress. Oxidative stress is associated with the progression and development of various chronic diseases as well as aging processes (Pizzino *et al.*, 2017; Vona *et al.*, 2021). Phenolic compounds found in parsley, such as flavonoids and phenolic acids, possess strong antioxidant properties by neutralizing free radicals by donating an electron,



Anti-inflammatory

- Parsley's flavonoids (e.g. apigenin and luteolin) can inhibit the production and activity of inflammatory mediators such as cytokines and prostaglandins.
- Apigenin can also inhibit the activity of enzymes involved in inflammations.
- Parsley's bioactive compounds may also influence the immune system and its response to inflammation.

Antimicrobial

- Parsley's essential oils (e.g. apiol and myristicin) or its phenolic compounds (e.g. chlorogenic acid and caffeic acid) can disrupt the integrity of bacterial cell membranes and inhibit bacterial growth.
- Parsley's flavonoids (e.g. apigenin and luteolin) may interfere with bacterial enzymes, inhibit bacterial DNA replication, or disrupt bacterial cell membranes.

Gut Microbiota Improvments

- Parsley's dietary fiber content (insoluble and soluble fiber like pectin), makes it a
 potential prebiotic.
- Parsley's antimicrobial properties can support a balanced gut microbiota by inhibiting harmful microorganism growth.
- Parsley may promote a healthy gut microbiota by reducing chronic gut inflammation.

Cholesterol-Lowering

- Parsley's flavonoids and polyphenols can inhibit cholesterol synthesis and promote its elimination from the body.
- The high level of antioxidants can prevent LDL cholesterol oxidation, thus reducing the risk of cardiovascular disease.
- Parsley's dietary fiber can help in lowering cholesterol levels.

Antioxidants

 Parsley is rich in antioxidants such as flavonoids (apigenin and luteolin), carotenoids (beta-carotene, lutein, and zeaxanthin), and vitamin C.

Figure 3. The possible mechanism of action of parsley (Petroselinum crispum) in promoting health benefits.

thereby alleviating their presence and reducing oxidative stress. Parsley's scavenging activity is found to reach 30–64% against 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical, the widely used indicator of antioxidant capacity (Al-Juhaimi and Ghafoor, 2011; Henning *et al.*, 2011; Hussain *et al.*, 2008). Another study demonstrated that parsley extract showed radical scavenging activity with a half-maximal inhibitory concentration (IC50) value of 3,310 µg mL⁻¹, indicating moderate to excellent antioxidant activity (Tang *et al.*, 2015).

Parsley's strong antioxidant potential is reported in various studies. In male rats exposed to hydrogen peroxide (H₂O₂) to induce oxidative stress, the oral administration of aqueous extract of parsley seeds at a dose of 8 mg 100 g⁻¹ body weight (BW) for 4 weeks reversed tissue damage. The results showed a significant elevation in the glutathione levels of plasma and tissues and a reduction in malondialdehyde levels (Khudiar et al., 2001). Consistently, a significant reduction in malondialdehyde levels was observed in hyperuricemic mice orally administrated with parsley juice at a dose of 5 mg 100 g⁻¹ BW daily for 2 weeks (Haidari et al., 2011). Similarly, in mice exposed to severe chronic oxidative stress, the daily consumption of 40% parsley for 7 days showed protective effects against oxidative damage by increasing cellular antioxidant enzymes, such as glutathione, catalase, and superoxide dismutase (Akinci et al., 2017). In other animal models, the administration of alcoholic extract of parsley reversed abnormalities observed due to dioxin, a highly toxic environmental pollutant.

Significant reductions in lipid peroxidation, protein carbonyl content, and nitric oxide were observed along with significant increase in antioxidant enzymes (El-Gayar et al., 2016). In the brain tissues of mice exposed to oxidative damage because of extensive doses of D-galactose, protective effects were observed after the administration of ethanolic extract of parsley leaves (Vora et al., 2009). Similar protective effects against oxidative damage were observed in animal models treated with parsley extracts (Guven et al., 2019; Vranješ et al., 2021). In mice models that experienced excessive fatigue, the administration of parsley extract, specifically its flavonoids, demonstrated significant anti-fatigue effects. These effects were potentially linked with the regulation of the Kelch-like ECHassociated protein 1-nuclear factor erythroid 2-related factor 2 (KEAP1/NRF2) and adenosine monophosphate-activated protein kinase-primordial germ cell-1α (AMPK/PGC-1α) pathways. Both these pathways play important roles in cellular homeostasis and adaptation to stress (Wang et al., 2022b). Nevertheless, further research is required to determine whether these findings could be replicated in humans.

Antiobesity effects

Parsley's beneficial effects in promoting weight loss or preventing lipid accumulation were examined in multiple studies. In a study conducted on obese women following a weight loss program, consuming parsley leaves accelerated their weight loss progression. The level of low-density lipoprotein (LDL) cholesterol was effectively reduced among those who consumed parsley in their daily diet. These results were attributed to a significant increase in females' serum antioxidant enzymes (Eshak and Mahran, 2018). In another study conducted with hypercholesteremic-induced mice, supplementation with 20% methanolic extract of parsley seeds significantly reversed increase in the levels of LDL with an increase in high-density lipoprotein (HDL) cholesterol (El Rabey et al., 2017). Similarly, in other hypercholesteremic-induced animal models, 10-20% of parsley was incorporated into animals' diet. The results showed that addition of parsley led to a significant reduction in body weight as well as rate of food efficiency. The histological examination also showed protective effects against liver lipid accumulation (El-Kherbawy et al., 2011). The observed effects were attributed to the dietary fiber content present in parsley, which contributed to the promotion of satiety and enhance food control (Dayib et al., 2020).

In addition, abundant supply of bioactive components in parsley, such as flavonoids and vitamin C, can exhibit antioxidant and anti-inflammatory effects, which have a vital role in supporting metabolic processes and potentially contribute to weight management (Abdali et al., 2015; Taherkhani et al., 2021). Antioxidant compounds are shown to enhance the metabolic system by positively influencing the activity and composition of the gut microbiota, which refers to the diverse community of microorganisms that reside in the gastrointestinal tract. Substances such as flavonoids are shown to stimulate the growth of beneficial bacteria while inhibiting the proliferation of harmful bacteria. Maintaining a balanced gut microbiota is recognized as a targeted strategy against obesity, and studies have shown that obese individuals often have reduced microbial diversity (Davis, 2016; Deledda et al., 2021; Duan et al., 2021; Sarmiento-Andrade et al., 2022; Wang et al., 2022a). On the other hand, some studies suggest that flavonoids may have antiobesity effects by improving insulin sensitivity and reducing blood glucose fluctuations (Al-Ishaq et al., 2019; Martín and Ramos, 2021). Thereby, parsley might indirectly support weight management by suppressing insulin resistance. Indeed, a couple of studies have reported reduced blood glucose levels in diabetic animal models because of parsley intervention (Bolkent et al., 2004; Sener et al., 2003). Improved insulin sensitivity is generally associated with better blood glucose control and a

reduced risk of developing obesity and related metabolic disorders (Clamp *et al.*, 2017).

Antidiabetic effects

Several studies have demonstrated the potential antidiabetic effects of parsley in induced diabetic animal models. In streptozotocin (STZ)-induced diabetic rats, the daily oral administration of parsley aqueous extract at the dosage of 2 g kg-1 BW for 28 days showed improvement in blood glucose levels. It also showed protective effects against the progressive alterations observed in rats' aorta and heart tissues caused by STZ injection (Sener et al., 2003). Similar protective effects on the heart tissue of diabetic rats were also observed after oral administration of parsley aqueous extract at a similar dosage (2 g kg-1 BW). Administration of parsley also showed a significant reversion in the hyperlipidemia caused by STZ injection (Soliman et al., 2015). Hepatoprotective effects were also observed in diabetic mice treated with parsley extract along with significant attenuation in blood glucose levels. The treatment reversed the progressive alterations observed in the hepatocyte tissue of diabetics along with reversing abnormalities in the levels of alanine aminotransferase (ALT) and alkaline phosphatase (ALP) that occurred due to STZ injection (Bolkent et al., 2004). Consistently, in other diabetic-induced animal models, parsley treatment showed hepatoprotective effects, comparable to glibornuride, a sulfonylureas antidiabetic drug. It was discovered that these effects were attributed to a reduction in nonenzymatic glycosylation process (Ozsoy-Sacan et al., 2006). Nonenzymatic glycosylation, also known as glycation, is a chemical reaction in which excessive glucose molecules bind to proteins or lipids in the absence of enzymatic activity. This process results in the formation of intricate and destructive substances known as advanced glycation end products (AGEs). Attenuating the formation of AGEs and effectively managing their impact has emerged as a therapeutic target in the comprehensive management of diabetes and its associated complications (Singh et al., 2014; Vlassara and Uribarri, 2014).

It was shown in another study that the oral administration of parsley extract promoted significant protective effects on the integrity of pancreatic β -cells (Eltablawy *et al.*, 2012). The observed effects were attributed to the rich composition of bioactive compounds found in parsley, such as polyphenols and phenolic acids. These components possess antioxidant, anti-inflammatory, and antiapoptotic properties, which contributed to preventing the destruction of β -cells (Babu *et al.*, 2013; Silveira *et al.*, 2019). Consequently, Sener *et al.* (2003) reported that the antidiabetic effects observed after the administration of parsley extract were accompanied by

a reduction in lipid peroxidation in protected tissues. Ozsoy-Sacan *et al.* (2006) also reported decreased lipid peroxidation and increased levels of lipid glutathione in diabetic rat models following treatment with parsley. Although these studies suggested the potential benefits of parsley in managing diabetes, further research is necessary to validate these findings and determine the precise mechanisms involved.

Hepatoprotective effects

The liver, the main detoxification organ, plays a crucial role in preventing diseases such as fatty liver disease, hepatitis, cirrhosis, and even certain cancers (Kalra et al., 2018). Parsley leaves were shown to promote hepatoprotective effects in multiple animal studies; in alcoholinduced hepatotoxicity in rat models, pretreatment with parsley's oil showed protective effects against the progressive damage caused by alcohol induction, including significant increases in the activities of serum ALT, ALP, and aspartate aminotransferase (AST) (Abou Seif, 2014). In another study, bile obstruction was performed to induce liver damage in rat models followed by oral administration of parsley extract at a dose of 2 g kg-1 for 28 days. A similar significant reduction in the levels of AST and ALT suggests the therapeutic potential of parsley leaves against liver fibrosis (Ede et al., 2023). Consistently, in other animal models induced with hepatotoxicity, the oral administration of parsley showed protective effects against liver lipid accumulation as well as inflammatory reactions (Ertaş et al., 2021). Similarly, administration of dietary parsley leaves at the dosage of 4 g kg⁻¹ per diet showed protective effects against zinc oxide-induced hepatotoxicity in fish models (Goda et al., 2023).

The hepatoprotective effects of parsley were shown to significantly relate to its properties in stimulating hepatocyte proliferation through up-regulation of hepatic apoptosis-related genes (Bastampoor et al., 2021). The lipid-lowering effects of parsley also have protective effects against lipid-induced liver injury (El-Kherbawy et al., 2011; Eshak and Mahran, 2018). Moreover, the beneficial effects of parsley against liver injury are attributed to its content of intensive nutraceutical agents, such as apigenin and myristicin. Both agents are shown to enhance detoxification ability of the liver by enhancing the activity of its enzymes involved in the process (Salehi et al., 2019; Seneme et al., 2021). In addition, the antioxidant effects of parsley have a role in promoting hepatoprotective effects. Pretreatment with parsley oil conducted by Abou Seif (2014) showed protective effects against hepatocytes' lipid peroxidation as observed by normalizing the levels of hepatic glutathione and catalase. Ede et al. (2023) observed similar results after the

administration of parsley extract to induce liver damage in mice models.

Nephroprotective effects

The kidneys are other vital organs for efficient detoxification by elimination of waste products, toxins, and excess fluids from the bloodstream. Maintaining healthy kidney function is crucial for sustaining optimal health and overall well-being (Li et al., 2020). Parsley leaves have a role in promoting promising functional effects to combat kidney injuries. In induced renal damages in rat models, administration of parsley extract at a dosage of 250 mg kg-1 BW showed significant reduction in the levels of kidney dysfunction serum markers, such as urea, creatinine, and uric acid. Protective effects against degeneration of kidney tissues were also observed (Ashry et al., 2021). Consistently, in ischemia/reperfusion-induced kidney injury in animal models, pretreatment with parsley extract at the doses of 100, 150, and 200 mg kg⁻¹ BW showed significant reduction in blood urea nitrogen as well as leukocyte infiltration (Roshankhah et al., 2019). Administration of parsley seed extracts was shown to reduce significantly urine protein content, indicating the kidney's efficiency in filtering and retaining proteins in the bloodstream, rather than allowing them to pass through urine; presence of protein in urine, a state known as proteinuria, is a sign of kidney damage or dysfunction (Gumaih et al., 2017).

The possible role of parsley in promoting nephroprotective effects depend on multiple mechanisms. One of the reported mechanisms is the excellent diuretic property of parsley, which means its ability to promote the production of urine and increase the frequency of urination, leading to eliminating toxins from the body. The diuretic property of parsley is attributed to its rich content of apiol, which is reported to induce vasodilation of renal arteries, thereby improving blood flow to the kidneys. Adequate blood supply is crucial for maintaining renal function and preventing kidney damage (Kreydiyyeh and Usta, 2002). Additionally, parsley leaves inhibit the formation of certain types of kidney stones, such as calcium oxalate stones (Al-Yousofy et al., 2017). Moreover, parsley's nephroprotective effects rely on its anti-inflammatory and antioxidant properties. Ashry et al. (2021) reported that the administration of parsley extract lessened abnormalities recorded in the levels of proinflammatory cytokines, including tumor necrosis factor-alpha (TNF- α) and interleukin-1 beta (IL-1 β), which occurred as a result of inducing renal damage in mice models. The authors also observed enhancement in oxidative parameters of the kidneys. Similar results were reported by Roshankhah et al. (2019), who showed enhancement in the kidney's oxidative parameters, including malondialdehyde and creatinine, after pretreatment to ischemia/reperfusion-induced kidney injury models with parsley extract.

Neuroprotective effects

The beneficial effects of parsley leaves on cognitive functions were investigated in multiple studies. In mice models exposed to cadmium toxicity, the daily administration of parsley juice at doses ranging from 5 to 20 g kg-1 BW showed significant lessening of behavioral changes caused by cadmium toxicity (Maodaa et al., 2016). Similarly, in mice dams exposed to cadmium, significant protective effects against developing behavioral changes were observed in their offspring with administration of parsley juice at doses of 20 and 10 mg kg⁻¹ BW. Improvement was observed in neurotransmitter levels, compared to positive control offspring (Allam et al., 2016). In mice models induced with Alzheimer's disease-like symptoms because of the treatment with scopolamine, an anticholinergic drug, the administration of parsley extract at a dosage of 2 g kg-1 BW for 2 weeks showed protective effects on spatial and recognition memory (Sener et al., 2022). These results were attributed to parsley's beneficial effects in enhancing brain's cholinergic functioning, which is a neurotransmitter working that uses neurotransmitter acetylcholine to transmit signals between neurons in the brain and other parts of the body. Şener et al. (2022) found that administration of parsley resulted in a reduced activity of acetylcholinesterase (AChE), an enzyme responsible for breaking down of acetylcholine. By inhibiting or reducing the activity of AChE, the breakdown of acetylcholine is slowed down, leading to increased levels of acetylcholine in the nervous system. Maintaining higher levels of acetylcholine can be considered a therapeutic target for treating certain cognitive conditions, including Alzheimer's disease.

The cholinergic activity of parsley is attributed to its content of apigenin (Salehi *et al.*, 2019). Other nutraceuticals present in parsley, such as myristicin, can promote neuroprotective effects by reducing oxidative stress (Ciftci *et al.*, 2014). It was found in Alzheimer's disease-induced mice that the administration of parsley extract effectively prevented oxidative damage in the lens tissues of the animals (Ertik *et al.*, 2023). Maodaa *et al.* (2016) reported that even at lower doses of 5 g kg⁻¹ BW, parsley administration exhibited protective effects against lipid peroxidation in neurons of the brain in mice models.

Anticancer effects

The protective effects of parsley leaves were further examined against proliferation of tumor in a couple

of studies. In mice fibroblasts (3T3-L1) cell lines, pretreatment with parsley extract at a dosage of 400 µg mL⁻¹ showed inhibition activity against DNA damage caused by induction of H₂O₂. The extract was also shown to inhibit cell migration of breast cancer cells (MCF-7) by nearly 40% (Tang et al., 2015). In a study using similar breast cancer cell lines, the anticarcinogenic properties of parsley were linked to the presence of phytoestrogen and its estrogen-like activity. However, the relationship between phytoestrogens and the incidence of breast cancer is complex and still under investigation (Schröder, 2021; Schroeder et al., 2017). The presence of apigenin and myristicin in parsley leaves could contribute to its anticarcinogenic properties. Both apigenin and myristicin are shown to regulate cell cycle in cancer cells by inhibiting its progression and inducing apoptosis, thereby preventing uncontrolled cell growth (Bao and Muge, 2021; Yan et al., 2017). However, additional studies are required to elucidate precise molecular pathways involved in parsley's anticarcinogenic effects and to thoroughly evaluate its effectiveness in treating or preventing cancer in clinical settings.

Anti-osteoporotic effects

The functional potential of parsley was investigated for its ability to combat bone health issues. In glucocorticoid-induced osteoporosis in mice models, administration of aqueous extract of parsley at a dosage of 2 g kg-1 BW for 8 weeks reversed the progressive decrease observed in bone mineral content and density. The results showed an increase in both calcium and phosphorus levels (Hozayen et al., 2016). Although parsley is not a direct source of essential bone-building nutrients, such as calcium and vitamin D, its potential to promote anti-osteoporotic effects might be attributed to its vitamin K content. Vitamin K plays a role in activating osteocalcin, a protein involved in bone mineralization. Maintaining adequate levels of vitamin K can support proper calcium utilization in bones (Akbari and Rasouli-Ghahroudi, 2018; Al-Suhaimi and Al-Jafary, 2020). In addition, magnesium and phosphate present in parsley may also contribute to the regulation of serum parathyroid hormone levels as well as acid phosphatase levels, both of which promote optimum bone health. Parathyroid hormone plays a crucial role in the maintenance of calcium balance, while acid phosphatase is responsible for the degradation of phosphoric acid esters (Alshami and Varon, 2020; Shaker and Deftos, 2023). Hozayen et al. (2016) reported that the observed anti-osteoporotic effects in mice were accompanied by normalization in the levels of serum parathyroid hormone and acid phosphatase. On the other hand, parsley's anti-inflammatory and antioxidant potential because of its richness in high-quality phytonutrients can have protective effects against developing osteoporosis. Recent studies have established a connection between the progression of osteoporosis and the presence of chronic inflammation and oxidative stress (Li *et al.*, 2023; Oršolić *et al.*, 2022).

Other effects

Further investigations for using parsley to combat other health conditions were conducted in multiple studies. One study reported antihypertensive effects of parsley's aqueous extract in hypertensive mice. The results indicated that parsley extract promoted vasodilation, which refers to the widening of blood vessels leading to a decrease in blood pressure (Ajebli and Eddouks, 2019). In another study, pretreatment with parsley's aqueous extract through intravenous administration showed antithrombotic effects in rat models subjected to induction of thrombosis. A reduction of 98% was observed in venous thrombus formation (Frattani et al., 2021). Furthermore, it was shown in another study that parsley's essential oil possessed antimicrobial properties against various strains (Linde et al., 2016). Extracts derived from parsley were found to exhibit antibacterial activity against pathogenic bacteria responsible for urinary tract infections (Petrolini et al., 2013) and bacteria associated with burn-related infections (Aljanaby, 2013). Abundance of phenolic compounds in parsley, in addition to their antioxidant properties, has been linked to its antibacterial effects (Wong and Kitts, 2006). The findings of these studies emphasized the potential health benefits of parsley and its extracts and highlighted the need for further exploration of parsley's practical applications in preventing and managing various health conditions. Continued investigations and execution of benefits of parsley could have a positive impact on public health and enhance the well-being of individuals globally.

Potential Toxicity and Safety Considerations

The use of parsley is generally regarded as safe for most individuals if consumed in moderate amounts. However, some studies have identified potential toxicity concerns and safety considerations associated with parsley consumption. An animal study investigating the effects of administration of ethanolic extract of parsley leaves reported mild hepatotoxic and nephrotoxic effects at doses $\geq 1,000$ mg kg $^{-1}$ BW. These findings suggested that the administration of parsley extract should be limited to an optimal dose (Awe and Banjoko, 2013). Additionally, it was indicated that individuals with calcium oxalate kidney stones should apply caution regarding parsley consumption, with an advised limit of not exceeding $1\frac{1}{2}$ cups of parsley because of its high content of calcium oxalate (Ajmera *et al.*, 2019).

Consumption of parsley was found to interfere with certain drug mechanisms. High content of vitamin K in parsley was shown to alter the effectiveness of warfarin (Coumadin) treatment, a commonly used anticoagulant. Additionally, excessive intake of parsley may interfere with diuretic therapy, leading to excessive water loss. Patients on aspirin therapy are also advised to avoid parsley consumption because of potential heightened sensitivity and allergic reactions. Moreover, the presence of myristicin has been associated with central nervous system effects. Ingesting excessive amounts of parsley has been linked to potential interference with opioid therapy, convulsions, and serotonin syndrome (Awe and Banjoko, 2013; Jakovljevic *et al.*, 2002).

Conclusions

The available studies indicated that parsley exhibits considerable potential in facilitating various favorable effects on health. These effects encompass its antioxidant and anti-inflammatory properties, its potential for management of diabetes, hepatoprotective and nephroprotective effects as well as its anticancer properties along with other potential health-promoting effects. These health benefits are largely attributed to the bioactive compounds present in parsley, which include a rich content of antioxidants, such as phenolic acids and flavonoids. Additionally, parsley contains key bioactive substances such as myricetin and apiol, which significantly contribute to its health-promoting properties. Parsley is also a rich source of essential vitamins, minerals, and dietary fiber, making it a substantial reservoir of nutrients and a highly valuable herb. Therefore, incorporating parsley into one's diet may prove to be a commendable addition for individuals seeking to enhance their overall health. However, it should be considered that the potential health benefits associated with parsley consumption could exhibit inter-individual variability. Therefore, it is crucial to avoid perceiving parsley as a remedy for all health issues. Seeking guidance from healthcare professionals or nutritionists is essential to develop a personalized approach, considering individual health requirements, medication interactions, and existing conditions. This promotes evidence-based and well-informed incorporation of parsley into a sustainable daily diet.

Author Contributions

Conceptualization: Albandari A. Almutairi, Hassan Mirghani Mousa, and Waheeba E. Ahmed. Literature research: Albandari A. Almutairi, Raghad M. Alhomaid, and Mona S. Almujaydil. Interpretation of data: Hassan Mirghani Mousa, Raghad M. Alhomaid, and Waheeba E. Ahmed. Visualization: Raya Algonaiman.

Writing—original draft preparation: Albandari A. Almutairi and Raya Algonaiman. Writing—review and editing: Raya Algonaiman. All authors had read and agreed to the published version of the manuscript.

Conflict of Interest

The authors declared that there were no conflicts of interest regarding the publication of this paper.

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