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Exploring nutritional value, phytochemical diversity, and medicinal potentials of almonds (*Prunus dulcis* Mill. D. A. Webb)

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Abstract

This review synthesises current research on the multifaceted benefits of almonds, highlighting their historical significance, nutritional profile, and medicinal properties. Originating from the Middle East and South Asia, almonds have traversed global culinary and medicinal landscapes, thanks to their rich content of monounsaturated fats, protein, fibre, vitamins, and minerals. The phytochemical diversity of almonds, including amygdalin, phenolic acids, and flavonoids, contributes to their antioxidant, anti-inflammatory, and cardioprotective effects. Advanced extraction and analysis methods reveal the complexity of almond's bioactive compounds, highlighting variability influenced by cultivar and environmental factors. Clinical trials and scientific studies support almonds' role in improving metabolic health, showcasing their potential in managing obesity, diabetes, and cardiovascular diseases, and even offering anticarcinogenic properties. Despite their health benefits, the review also addresses the allergenic potential of almonds and the importance of management and labelling regulations for sensitive individuals. Future research directions emphasize the need to explore the mechanistic basis of almonds' health benefits, develop sustainable cultivation and processing methods, and investigate the potential for new pharmacological discoveries.

1. Introduction

Almonds (*Prunus dulcis* Mill. D. A. Webb), characterized by their sweet and rich taste, hold a venerable place in the annals of history and the world's pantheon of nutritious foods. This revered nut, encapsulated within a hard shell, has been a symbol of life, health, and sustenance across cultures and civilizations. The almond tree, with its white to pale pink flowers, is native to the Middle East and South Asia. However, its cultivation has spread widely, adapting to various climates and regions, making almonds a global staple (Hussain *et al.,* 2021). The historical significance of almonds can be traced back thousands of years (Esfahlan *et al.,* 2010). Ancient texts and archaeological findings suggest that almonds were among the earliest cultivated foods, which contributed to the spread of trade along the silk road between Asia and the Mediterranean (Gradziel, 2017). Almonds were highly prized in the diets of ancient Egyptians, Romans, and Greeks, who recognized their nutritional value and incorporated them into their cuisine and rituals (Bryant *et al.,* 2014). For example, the Romans showered newlyweds with almonds as a symbol of fertility (Edwards, 1996). In the Bible, almonds are mentioned numerous times, symbolizing watchfulness and promise due to the almond tree's early flowering (Lehner *et al.,* 2003).

Almonds have not only been celebrated for their taste but also for their medicinal properties. Traditional medicine systems, such as Ayurveda in India and Unani in the Middle East, have long prescribed almonds for their health benefits, including improving brain health, enhancing vitality, and supporting the body's healing processes (Siddiqui and Begum, 2023; Pandey *et al.,* 2013). The oil extracted from almonds was used by ancient Chinese and Ayurvedic practices to treat dry skin conditions and improve hair health, showcasing the nut's versatility (Ahmad, 2010). Geographically, the distribution of almonds is now vast, spanning several continents. The United States, specifically California, has emerged as the largest producer of almonds, thanks to its suitable climate and advanced agricultural practices (Barreca *et al.,* 2020). The state's Central Valley offers the perfect combination of warm weather and rich soil, contributing to over 80% of the world's almond supply (Gebremichael *et al.,* 2021). Other significant almond-producing countries include Spain, Italy, Australia, and Morocco, each contributing to the global almond market with their unique varieties (Campos *et al.,* 2023).

The Mediterranean region; however, holds a special place in the almond's cultivation history. The almond trees thrive in the Mediterranean climate, with its mild, wet winters and hot, dry summers. This region is renowned for producing almonds that are rich in flavour, which are often used in local cuisines, sweets, and snacks (Gradziel *et al.,* 2017). As almonds have traversed from their native habitats to become a global agricultural commodity, their nutritional profile has garnered attention from the scientific community and health enthusiasts alike. Rich in monounsaturated fats, protein, fibre, and essential vitamins and minerals such as vitamin E, magnesium, and potassium, almonds offer myriad health benefits. These range from lowering cholesterol levels and managing blood sugar to reducing the risk of heart disease and supporting weight management efforts (Barreca *et al.,* 2020).

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1.1 Importance in diet and traditional medicine

The incorporation of almonds into dietary practices spans centuries, bridging the gap between ancient wisdom and modern scientific inquiry. Both historical texts and contemporary research emphasize the multifaceted benefits of almonds in diet and traditional medicine, reinforcing their status as both a nutritious food and a therapeutic agent. In the field of dietetics, almonds have been celebrated for their nutrient density, offering a rich source of manganese, vitamin E, copper, magnesium, fibre, phosphorus, monounsaturated fatty acids, riboflavin, and protein. Researchers elucidate that despite almonds' high-fat content, their inclusion in diets has been associated with reduced low-density lipoprotein (LDL) cholesterol concentrations and weight management benefits, without adversely impacting insulin sensitivity. Furthermore, their analysis posits almonds as an excellent source of bioavailable α-tocopherol, which enhances the resistance of LDL against oxidation, positioning almonds as a heart healthy food choice (Chen *et al.,* 2006).

Almonds' role in mitigating cardiovascular disease risks through lipid profile improvement has been substantiated in various studies. The constant LDL-C-lowering impact of almonds was addressed by researchers concerning healthy persons as well as those with high cholesterol and diabetes. The mechanisms proposed for this effect encompass almonds' nutritional composition, which targets primary routes of LDL-C reduction, such as decreased (re)absorption of cholesterol and bile acid, and increased LDL-C receptor activity (Berryman *et al.,* 2011). The intersection of almonds with traditional medicine reveals a longstanding appreciation for their health-promoting properties. In Persian medicine, almonds have been revered for their Muqawwi dimagh (brain tonic) qualities, among other benefits. This traditional use aligns with modern findings on almonds' neuroprotective, anti-inflammatory, and cardiometabolic protective effects, further exemplified by research on their prebiotic, antimicrobial, and antioxidative capacities (Siddiqui and Begum, 2023).

Recent clinical trials have expanded the understanding of almonds' therapeutic potential. The authors found that eating almonds during caloric restriction significantly lowered blood pressure and truncal fat in those who were overweight or obese, suggesting the benefit of almonds for improved metabolic health (Dhillon *et al.,* 2016). Almonds have also been shown to be effective in treating chronic illnesses; in patients with type 2 diabetes mellitus, it was shown that almond consumption improved lipid profiles and glycemic management (Li *et al.,* 2011). The prebiotic properties of almonds have also been explored, with studies noting their influence on gut microbiota composition and function. Almonds have been found to promote the growth of beneficial bacteria, contributing to overall gut health and, by extension, systemic health benefits (Ren *et al.,* 2020).

2. Phytochemistry of almonds

2.1 Primary phytochemical compounds found in almonds

Almonds (*Prunus dulcis* Mill. D. A. Webb), cherished for their nutritional benefits, are also a reservoir of a wide range of phytochemical compounds that contribute to their health-promoting properties. The phytochemistry of almonds is complex, encompassing a variety of bioactive molecules such as amygdalin, phenolic acids, flavonoids, and fatty acids, each playing a unique role in contributing to the nut's antioxidant, anti-inflammatory, and cardioprotective effects (Karimi *et al.,* 2021). Amygdalin, a cyanogenic diglucoside, is found predominantly in bitter almond varieties. While it is less prevalent in sweet almonds, the ones commonly consumed, its presence has sparked interest due to its potential anticancer properties, although its efficacy and safety remain subjects of ongoing research (Lee *et al.,* 2013). Phenolic acids and flavonoids in almonds, particularly in their skins, are potent antioxidants. Researchers identified a vast array of phenolic compounds in almond skins, including flavanols, flavonols, dihydroflavonols, and flavanones. These compounds, such as quercetin, kaempferol, and catechin, contribute significantly to the nut's antioxidant capacity, which has been linked to reduced risk of chronic diseases including heart disease and diabetes. The diversity of these compounds highlights the nut's complex phytochemical profile, which can vary based on almond genotype and environmental factors during growth and post-harvest processing (Monagas *et al.,* 2007).

Almonds are also rich in essential fatty acids, which constitute about 50% of the nut's weight, primarily in the form of monounsaturated fatty acids (MUFA), particularly oleic acid. This lipid profile is beneficial for cardiovascular health, as it can help reduce LDL cholesterol levels and maintain healthy blood vessels (Yada *et al.,* 2011). Furthermore, almonds contain other bioactive molecules such as phytosterols and squalene, which further contribute to their health-promoting effects. For example phytosterols have been shown to reduce cholesterol, while squalene, a triterpene, has been investigated for its antioxidant and perhaps anticancer effects (Roncero *et al.,* 2020). The phytochemical abundance of the nut is determined by several variables, such as the kind of almond, the circumstances under which it is grown, and the procedures used during processing. For example, deficit irrigation strategies have been shown to affect the concentrations of bioactive compounds in almonds, potentially enhancing their nutraceutical value. Analogously, processing methods like roasting and blanching may change the antioxidant capacity and phenolic profile of almonds, changing the health benefits (Prgomet *et al.,* 2019).

2.2 Methods of phytochemical extraction and analysis

Several techniques are used in the extraction and analysis of phytochemical substances from almonds to separate and characterize the wide range of bioactive chemicals that are present. These substances, which include flavonoids, phenolic acids, and other antioxidants, greatly add to the health benefits of almonds. To better use almond by-products and increase the nut's value, sophisticated extraction and analytical procedures have been developed to effectively extract and evaluate these components.

2.2.1 Microwave assisted extraction (MAE)

The use of Microwave assisted extraction (MAE) has improved the process of extracting phenolic compounds from residual almond skin. This emphasizes the significance of factors such as the weight of the almond skin, microwave power, and duration of irradiation. The optimal extraction conditions for this method, which demonstrates the potential of almond skin as an abundant reservoir of phenolic compounds, consist of 4 g of almond skin, a 60-second extraction time, 100 Watts of power, and 60 milliliters of 70% ethanol. This approach showcases the diversity among different varieties of almonds by emphasizing the efficacy of MAE in extracting bioactive compounds, as well as the influence of cultivar species on polyphenol concentration and antioxidant properties (Valdes *et al.,* 2015).

2.2.2 Ultrasound assisted extraction (UAE)

The rapid, environmentally friendly, and easy method of extracting antioxidant phenolic compounds from Moroccan almond cold-pressed oil leftovers is known as ultrasound aided extraction (UAE). Compared to traditional approaches, this strategy significantly improves extraction efficiency by using aqueous ethanol as a green solvent and using ultrasonic frequency for an optimal period. The method's effectiveness is attributed to the optimization of parameters such as solvent concentration, extraction time, and ultrasound frequency, which lead to a substantial gain in terms of extraction efficiency. The effective implementation of this approach on various indigenous almond genotypes indicates its capacity to produce extracts exhibiting antioxidant properties, which could be utilized in nutraceutical and cosmetic formulations (Tungmunnithum *et al.,* 2020).

2.2.3 Solid phase extraction (SPE)

For the characterisation of complicated phenolic combinations, such as those present in almond extracts, solid phase extraction (SPE) has been used. The efficiency of SPE methods, such as reverse-phase and mixed-mode SPE, in the separation and purification of oligosaccharides and peptides has been assessed. In particular, mixed-mode SPE has shown potential in collecting and maintaining small/hydrophilic peptides in the high-organic fraction, hence allowing the identification of a greater number of oligosaccharides and dipeptides in almond extracts. This analytical procedure may be used for the investigation of phenolic compounds with low and high molecular mass in natural goods, providing information on the health advantages and bioactivity of almonds and other nuts (Bolling *et al.,* 2011).

2.2.4 Liquid chromatography coupled with high-resolution mass spectrometry (LC-HRMS) and gas chromatography-mass spectrometry (GC-MS)

Almond extracts rely on nontargeted metabolomic approaches to evaluate their antioxidant activity and metabolite composition, and they play a crucial role in this process. With the use of these methods, the almond metabolome may be thoroughly examined, revealing a variety of substances that support the nut's antioxidant qualities. Almonds have the potential to be a source of antioxidant recovery due to the association between their phytochemical content and antioxidant activity; however, certain extraction techniques seem to maximize the amount of antioxidants that may be recovered from almonds (Kaneria *et al.,* 2018).

These advanced methodologies underline the complexity and richness of the phytochemical profile of almonds, emphasizing the importance of optimizing extraction and analysis conditions to fully exploit the health-promoting potential of this nut.

2.3 Variability of phytochemical compounds in almonds: Influences of variety and growing conditions

Almond variety (cultivar) and growing circumstances have a major impact on the heterogeneity of phytochemical compounds in almonds, indicating the complex interaction between genetics and environmental variables in shaping the nutritional and phytochemical profile of almond nuts. This variability has important implications for both almond cultivation practices and the selection of varieties for specific health benefits or food uses.

2.3.1 Variability due to almond variety

Almond varieties exhibit considerable genetic diversity, which is reflected in their chemical compositions. A comprehensive study highlighted that no single almond compound could serve as a universal biomarker to differentiate among almond cultivars. Instead, a combination of macronutrients, tocopherols, phytosterols, polyphenols, minerals, amino acids, and volatile compounds, alongside DNA fingerprinting, has been suggested for distinguishing almond cultivars and origins (Beltrán *et al.,* 2021). This diversity is not only crucial for avoiding fraud in protected geographical indications but also for selecting cultivars that are nutritionally superior or better suited for specific food applications.

2.3.2 Environmental effects on phytochemical compounds

Environmental conditions, including the specific climatic conditions of the growing area, significantly affect the phytochemical composition of almonds. Research has shown that differences in the nutritional content between and within almond cultivars may occur depending on the year of harvest and the orchard's geographic location. Almonds, for instance, have very comparable macro- and micronutrient profiles across cultivars, with minor variations based on growing area and harvest year. Considerable variations in nutritional content were noted for each nutrient as a result of growing area, year, and/or variety (Yada *et al.,* 2013).

2.3.3 Influence of harvest time and cultivar

The influence of harvest timing on the nutritional and chemical makeup of almonds differs throughout cultivars as well. For example, during ripening, the quantity of fat and protein reduced while the content of lipids rose. During ripening, the fatty acid content exhibited non-uniform behaviour, with the cultivar having a significant impact. Antioxidant activity and total phenolic compounds varied across cultivars but typically increased throughout ripening, suggesting that antioxidant production also takes place in the latter stages of ripening (Summo *et al.,* 2018).

2.3.4 Irrigation and its impact

Almonds may contain more beneficial nutrients when grown using irrigation deficit techniques like controlled deficit irrigation (RDI) or sustained deficit irrigation (SDI), which reduce water flow to the plants. For instance, the season had a greater impact on the synthesis of the most abundant phenolics in almond hulls and skins-naringenin-7-O-glucoside and isorhamnetin-3-O-rutinoside than the irrigation treatment. However, the synthesis of individual phenolics was more responsive to seasonal variations than to irrigation treatments, indicating the complex interaction between environmental factors and phytochemical synthesis (Prgomet *et al.,* 2019).

3. Pharmacokinetics of phytochemicals present in almond

Although direct studies on the ADME processes specific to almond phytochemicals are limited, research on similar phytochemicals can provide insights into how these processes might occur for almond constituents. Almond phytochemicals, particularly polyphenols, are absorbed in the gastrointestinal tract, but their bioavailability can vary significantly. For instance, studies have shown that the bioavailability of flavonoids, a class of polyphenols abundant in almonds, is generally low due to their poor absorption, extensive metabolism, and rapid excretion. The presence of almond skin can influence the absorption rates of these polyphenols due to the interaction with intestinal microbiota and enzymes that may enhance the conversion of polyphenols to more bioavailable forms (Urpi-Sarda *et al.,* 2009). The metabolism of almond phytochemicals mainly occurs in the liver, where they undergo phase I (functionalization reactions) and phase II (conjugation reactions) metabolic transformations. These transformations are crucial for increasing the solubility of phytochemicals for their eventual excretion. Research has highlighted the importance of gut microbiota in the metabolism of almond polyphenols, producing a wide range of metabolites that may possess different biological activities from their parent compounds (Tulipani *et al.,* 2012).

Significant influence is exerted by particle size during the initial phase of digestion on the release of components necessary for their absorption and metabolism. Mastication affects nutrient assimilation and absorption in the intestines, hormone release, weight management, and satiety, among other substances including proteins, carbohydrates, and lipids. Very few variations were found among the masticated bolus of raw almonds and roasted almonds throughout the duodenal phase in terms of lipid release in the digestive compartment and lipid digestion time course (Grundy *et al.,* 2015*a*; Grundy *et al.,* 2015*b*). *In vivo,* pig experiments with raw and roasted almonds revealed no statistically significant differences in plasma glucose or lipid amounts, particle sizes, or rheological behaviour during gastric digestion. However, the authors did find that the pigs' gastric emptying of protein was faster with raw almonds than with roasted ones, which they attributed to protein segregation (Bornhorst *et al.,* 2014; Bornhorst *et al.,* 2013).

The particle size has a notable impact on the early stage of digestion, affecting the release of essential components required for absorption and metabolism. Mastication impacts the process of food digestion and absorption in the intestines, as well as hormone release, weight control, and satiety. It also affects the breakdown of components such as proteins, carbs, and fats. Further work has shown a possible method *via* which nutrients may not be properly absorbed in the gastrointestinal tract: the occurrence of almond cell walls, which hinder the expulsion of lipids from intact cells. Moreover, recent researchers have shown the crucial role of almond cell walls in controlling almond components, the increase of fat in the blood after a meal, and blood sugar levels, leading to a decrease in risks such as heart disease (Mandalari *et al.,* 2014).

Almonds are abundant in polyphenols, which undergo remarkable metabolism following ingestion; the bioavailability of these compounds has a substantial impact on the health-enhancing characteristics of the almond matrix, in addition to its derivatives and co-products. Indeed, the process of polyphenol metabolism can generate various categories of metabolites, frequently possessing more intriguing biological properties than the natural precursors found in foods. Almond tannins, for instance, are mostly used and converted by the gastrointestinal microbiota once proanthocyanidins are broken down, producing hydroxybenzoic acids and valerolactone intermediates. After this metabolic process, the products are absorbed by the gut microbiota and undergo enzymatic modification to produce hydroxyl, glucuronic, sulfate, and/or methylated derivatives. Studies investigating the bioavailability of polyphenols from almonds in humans after ingesting whole almonds or their crude extracts are also available (Mandalari *et al.,* 2014).

4. Pharmacological properties

4.1 Antioxidant and anti-inflammatory effects

Extensive research has been conducted on the potential health benefits of almonds, with a specific focus on their anti-inflammatory and antioxidant properties. Almonds predominantly possess antioxidant properties by virtue of their flavonoid and vitamin E (α-tocopherol) content, which scavenge free radicals and safeguard cells against oxidative harm. Almond consumption decreased oxidative stress biomarkers, including lipid peroxidation and oxidative DNA damage, in male smokers, according to one study. The findings of this research indicate that smokers' antioxidant defenses were strengthened and biomarkers of oxidative stress were reduced when almonds were included in their diet. These results suggest that almonds may have the capacity to alleviate the oxidative damage that is linked to smoking (Li *et al.,* 2007). Moreover, it has been shown that the flavonoids and polyphenols found in almond skins work in concert with vitamins C and E to strengthen low-density lipoprotein's (LDL) resistance to oxidation. This synergistic action highlights the unique contribution of almond polyphenols to the overall antioxidant capacity of the nut and its potential to prevent cardiovascular diseases by inhibiting LDL oxidation (Chen *et al.,* 2005). Researchers investigated the effects of almond skin polyphenols (ASP) on oxidative stress biomarkers in humans. It reveals that ASP intake enhances plasma antioxidant capacity and modulates enzymes involved in oxidative defence, suggesting potential health benefits against oxidative stress-related diseases (Chen *et al.,* 2019). Further, the research assesses phenolic content and antioxidant power in Spanish almonds, finding significant variances among 11 genotypes. It emphasizes the genotype's strong influence on antioxidant capacity and phenolic compounds, with Belona, Guara, and Vialfas showing higher levels, suggesting quality implications for these almond varieties (Moreno *et al.,* 2021).

Anti-inflammatory properties have also been demonstrated in almonds; these properties are vital for preventing chronic inflammatory diseases. Almond intake has been associated with lower levels of inflammatory biomarkers such as C-reactive protein (CRP) and interleukin-6 (IL-6). A meta-analysis found that eating almonds significantly lowered blood concentrations of IL-6 and CRP, indicating that almonds may help lower adult inflammatory levels (Fatahi *et al.,* 2021). Furthermore, studies on the anti-inflammatory qualities of polyphenols from almond skin have been conducted in both *in vitro* and *in vivo* models, with encouraging results. For example, in differentiated 3T3-L1 adipocytes, almond skin polyphenol extracts increased lipolysis and reduced the inflammatory response, indicating prospective uses for almond polyphenols in the management of inflammation associated with obesity (Huang *et al.,* 2017). Further, the study examined the anti-inflammatory effects of aqueous extracts and n-hexane fractions from *P. dulcis* seeds. It demonstrates that these extracts stabilize erythrocyte membranes and inhibit protein denaturation, suggesting a potential therapeutic role for almond seed components in managing inflammation (Olatunde *et al.,* 2022).

4.2 Cardioprotective benefits and implications for blood lipid profiles

The cardioprotective benefits of almond consumption and its implications for blood lipid profiles have been the focus of numerous studies, revealing almonds' potential to promote heart health and manage lipid-related disorders. A randomized controlled trial examined the effect of almond intake on lipid profiles across different body mass indexes (BMIs). The study found that regular almond supplementation resulted in lowered cholesterol, LDL (low-density lipoprotein), and VLDL (very-low-density lipoprotein) levels in normal-weight individuals, while also noting lowered cholesterol levels in overweight participants. This suggests that almonds can positively impact lipid profiles, with effects being more pronounced in individuals of normal weight compared to their overweight or obese counterparts (Tahir *et al.,* 2019). Researchers looked at how eating almonds affected metabolic risk factors including glucose metabolism and hyperinsulinemia, as well as lipid profiles. The intake of almonds was shown to dramatically lower levels of total cholesterol, LDL-C, and HbA1c in young adults and adolescents who are at risk of developing diabetes. The potential of almonds in preventing pre-diabetes and its related problems is highlighted by this research (Madan *et al.,* 2021). The most common complications of diabetes include neuropathy, nephropathy and retinopathy (Hashim *et al.,* 2023; Hashim *et al.,* 2024; Stitt *et al.,* 2016).

A separate investigation documented that healthy adults who consumed whole almonds as a refreshment for six weeks experienced enhancements in endothelial function and reductions in LDL cholesterol, but no discernible impact on liver fat or other cardiometabolic risk factors. This finding highlights the specific benefit of almonds in enhancing cardiovascular health through improved endothelial function and lipid reduction (Dikariyanto *et al.,* 2020). Furthermore, the systematic review and meta-analysis confirmed the significant outcomes of almond or almond oil consumption in lowering blood lipid levels. The review included 40 clinical trials, with almond intake ranging from 10 to 100 g/day, and found consistent evidence supporting almonds' lipid-lowering effects (Osman and Al-Naggar, 2023). Researchers examined the cardiomodulatory effect of almond-citrus peel-fortified shortbread on hyperlipidemic hypertensive rats. The study found significant improvements in blood cholesterol, triglyceride levels, and various cardiovascular health markers, suggesting the potential therapeutic benefits of almond consumption in managing hyperlipidemia and hypertension (Ademosun *et al.,* 2023). These studies collectively reinforce the understanding that almonds can play a beneficial role in cardiovascular health by modulating lipid profiles. Regular almond consumption is associated with reductions in total cholesterol, LDL-C, and other risk factors for cardiovascular diseases.

4.3 Antidiabetic effects and influence on glycemic control

An investigation that employed a systematic review and meta-analysis to examine the impact of almonds on inflammatory markers, gut microbiota, and glycometabolism in individuals diagnosed with type 2 diabetes determined that diets containing almonds substantially reduced glycated haemoglobin (HbA1c) and body mass index (BMI), but had no significant effect on fasting blood glucose, postprandial blood glucose, or other inflammatory biomarkers. This implies that almonds could potentially enhance the management of diabetes *via* mechanisms other than direct glucose regulation, which could be associated with their low glycemic index and dietary fibre content (Ojo *et al.,* 2021). Males with type 2 diabetes were the subjects of an additional investigation that examined the immediate impacts of almonds on postprandial glycemic, hormonal, and appetite reactions. Almonds have the potential to positively modulate postprandial glucose and insulin levels, as evidenced by the fact that a meal containing almonds led to decreased glycemic and insulinemic responses and elevated postprandial GLP-1 serum concentrations (Bodnaruc *et al.,* 2020).

An additional measure of the positive aspects of almond consumption was examined in a randomized controlled trial that examined the impact of a low carbohydrate diet containing almonds on type 2 diabetes patients' glycometabolism, intestinal microbiota, depression, and GLP-1 levels. The study found significant improvements in depression and HbA1c levels, suggesting that almonds' effects on glycometabolism and mental health may be mediated through alterations in gut microbiota and GLP-1 secretion (Ren *et al.,* 2020). The purpose of the research was to determine if almonds may help overweight Asian Indian people with their lipid profile and reduce insulin resistance. After consuming almonds, the oral insulin disposition index, insulin resistance measurements (HOMA-IR), and total cholesterol significantly improved, according to this randomized controlled experiment. These results suggest that daily intake of almonds may enhance insulin sensitivity and lipid metabolism, potentially aiding in the management of diabetes and its related risks in a population with a high predisposition to these conditions (Gayathri *et al.,* 2023).

Another study explored the potential benefits of almonds in managing diabetes-related erectile dysfunction. The research highlighted the influence of almond consumption on oxidative stress markers, smooth muscle/collagen ratio, and sexual function in diabetic male rats. Findings indicated that almond supplementation could mitigate some of the complications associated with diabetes, such as erectile dysfunction, through antioxidative effects and improvements in tissue health. This study opens avenues for further research into almonds' nutraceutical use in sexual health and diabetes management (Adebayo *et al.,* 2022; Gupta *et al.,* 2022; Staines *et al.,* 2023). Later studies looked at how eating almonds affected metabolic risk factors in young adults and adolescents who are at risk of developing pre-diabetes, such as glucose metabolism and hyperinsulinemia. The results of the randomised controlled trial demonstrated that eating almonds significantly lowered the levels of total cholesterol, LDL cholesterol, and HbA1c. This emphasizes how almonds may help younger individuals at risk prevent diabetes and its aftereffects (Madan *et al.,* 2021).

4.4 Potential anticarcinogenic properties and mechanisms

The potential anticarcinogenic properties and mechanisms of almonds have been a topic of interest in recent research, with studies exploring various aspects of how almonds might contribute to cancer prevention and therapy. An investigation was conducted on the effects of phenolic-rich extracts from the hulls of almond (AHE) and walnut (WHE) on the migration, apoptosis, and proliferation of bone tumour cells. The extracts' potential anticancer effects were suggested by the way their polyphenolic chemicals activated caspase, reduced mitochondrial membrane potential, and inhibited tumour cell growth in a dose-dependent manner (Khani and Meshkini, 2020). Furthermore, utilizing both *in vivo* and *in vitro* experiments, a different study examined the antiangiogenic properties of *P.dulcis* oil alone and in combination with aspirin. The findings showed that sweet almond oil significantly inhibited the growth of blood vessels, particularly when paired with aspirin. This implies that the use of sweet almond oil as an anti-angiogenic medication may be possible in the management of cancer (Ali and Sahib, 2022).

Research focused on the chemical composition of Italian almond cultivars and their antioxidant properties. The study highlighted the presence of various compounds in almonds, such as cyanogenic glycosides, flavonoids, and diterpene glycosides, which possess antioxidative properties potentially beneficial in preventing cancer (Bottone *et al.,* 2020). Another study assessed how roasting and blanching processing treatments affected the bioactive compounds and antioxidant activities of almonds. The results indicated that roasting generally increased levels of bioactive compounds and antioxidant activities, potentially enhancing almonds' anticarcinogenic properties (Oliveira *et al.,* 2020).

Investigating the impact of irrigation treatments on almonds, researchers found that deficit irrigation led to variations in phytoprostanes and phytofurans levels, which are markers of oxidative stress and possess biological properties beneficial for human health, including anticarcinogenic potential (Lipan *et al.,* 2020). While focusing on antiobesity effects, another study provides insights into almonds' broad health benefits, including potential anticarcinogenic properties. Almond supplementation reduced body weight and improved lipid profiles in animals, suggesting a holistic health benefit that could extend to cancer prevention (Asdaq *et al.,* 2021). These studies collectively underline the potential of almonds and their bioactive compounds in offering anticarcinogenic benefits, whether through direct antiproliferative and apoptosis-inducing effects, antiangiogenic activities, or through antioxidant properties that could mitigate cancer risk.

4.5 Effects on weight management and satiety

Almonds have gained attention for their potential benefits in weight management and satiety, and recent research further supports their role in dietary regimens aimed at controlling weight and enhancing feelings of fullness. An analysis of 64 randomized controlled trials and 14 systematic reviews/meta-analyses conducted a narrative review, emphasizing that almonds while being high in energy density, had the effect of a lower energy-dense diet when ingested. Almonds were linked to a modest although noteworthy reduction in average body weight and fat content, perhaps because they promote feelings of fullness, reduce the amount of energy absorbed from macronutrients, and boost resting energy expenditure. The research also indicates the rising health advantages of almonds in terms of cognitive function and the costs associated with medical treatment for cardiovascular disease (Dreher, 2021). A further study compared raw almonds with savory crackers and water as mid-morning snacks and found that almonds resulted in a lower overall hunger drive. Almonds reduced hedonic desire for high-fat meals even though there was no discernible change in 24-hour calorie intake, suggesting that they are useful in regulating hunger over a whole day (Hollingworth *et al.,* 2019). Another randomised controlled trial demonstrated that a balanced hypocaloric diet enriched with almonds led to significant reductions in body weight, BMI, waist and hip circumferences, and improvements in lipid profiles compared to an almond-free diet, suggesting that almonds can be a beneficial addition to weight reduction diets (Ünal and Pekcan, 2020).

Over a year-long trial, participants who consumed almonds instead of biscuits did not experience adverse effects on body weight and composition but saw improvements in diet quality. This indicates that almonds can be included in long-term dietary plans without negative impacts on weight while improving nutritional intake (Brown *et al.,* 2022). A study found that almond consumption led to changes in microbiota composition, increased bacterial richness, evenness, and diversity, and decreased stool pH and moisture content, which could have implications for weight management and gut health (Choo *et al.,* 2020). Studies have shown that adding almonds to a Mediterranean diet affects the biology of both subcutaneous and visceral adipose tissue. This is done by promoting the growth of tiny fat cells and increasing the activity of genes involved in the formation of fat cells and blood vessels. This indicates that almonds may have a role in improving the malfunction of white adipose tissue associated with obesity (Osorio-Conles *et al.,* 2022).

4.6 Bone health benefits due to minerals and vitamins

Almonds are celebrated not just for their rich nutrient profile, but also for their potential benefits to bone health, largely attributable to their content of minerals and vitamins crucial for bone structure and strength. A comprehensive review underlines almonds' richness in essential nutrients including calcium, magnesium, phosphorus, and vitamin E, all recognized for their roles in bone health. The study also notes almonds' beneficial effects on metabolic health markers, which indirectly support bone health by improving overall health status and reducing inflammation, a known risk factor for bone loss and osteoporosis (Barreca *et al.,* 2020). While not focused exclusively on almonds, the chapter emphasizes the importance of dietary sources of calcium, magnesium, and vitamin D for maintaining bone health. Given almonds' composition, incorporating them into the diet can contribute to meeting the nutritional needs for these essential bone-supporting nutrients (Sánchez-Rodríguez *et al.,* 2021)

Researchers explored the impact of vitamin A on bone health, suggesting that while excessive intake can have negative effects, adequate intake supports bone health. Almonds, being a source of vitamin E, indirectly contribute to a balanced intake of fat-soluble vitamins, including vitamin A, by promoting their absorption and utilization due to their healthy fat content (Yee *et al.,* 2021). Though primarily focused on gastrointestinal health, a review indirectly supports the role of almonds in bone health through the promotion of gut health. A healthy gut can enhance the absorption of bone-promoting minerals and vitamins from the diet, including those found in almonds (Mandalari *et al.,* 2023). Further study focusing on oxidative stress markers in almonds, suggests the potential for almonds to contain compounds that could contribute to reducing oxidative stress, a factor in bone health. The presence of bioactive compounds in almonds, influenced by agricultural practices, highlights the nut's complex nutritional profile beneficial to bone health (Lipan *et al.,* 2020).

5. Nutritional profile of almonds

Around half of the weight of almonds consists of fat, mostly monounsaturated fatty acids (MUFA), which are known to lower levels of low-density lipoprotein cholesterol (LDL-C). Consequently, almonds are linked to advantages for cardiovascular well-being and disorders connected to obesity. However, they may be a hazard for persons who are possibly allergic. A research assessed the levels of â-sitosterol, stigmasterol, and campesterol in seven almond kinds, which are among the top 10 almond varieties in California. The amount of â-sitosterol varied from 103 to 206 mg/100 g, stigmasterol ranged from 1.3 to 9.8 mg/100 g, and campesterol ranged from 4.1 to 11.8 mg/100 g (Yada *et al.,* 2013). Nestled among tree nuts, almonds are acknowledged as a nutritious snack and are abundant in protein, monosaturated fatty acids, dietary fibre (with a 4:1 ratio of insoluble to soluble fiber), vitamin E, riboflavin, and vital minerals (Chen *et al.,* 2006; Yada *et al.,* 2013). Furthermore, the researchers determined that there was less than a 1.2-fold variation in mean protein, total lipids, fatty acids, and dietary fibre amongst the seven almond species investigated. The greatest changes across types were reported in riboflavin (Yada *et al.,* 2013). In exploring the diverse health benefits of almonds, Table 1 provides a comprehensive summary of their pharmacological properties.

Table 1: Overview of pharmacological properties and health benefits of almonds

Pharmacological property	Key findings	References
Antioxidant and anti-inflammatory effects	Almonds contain vitamin E, flavonoids, and phenolic compounds that provide antioxidant and anti-inflammatory benefits.	Li *et al.*, 2007; Chen *et al.*, 2005; Huang *et al.*, 2017; Fatahi *et al.*, 2021
Cardioprotective benefits	Regular almond consumption can improve lipid profiles, potentially reducing cardiovascular disease risk.	Tahir *et al.*, 2019; Dikariyanto *et al.*, 2020; Osman and Al-Naggar, 2023; Ademosun *et al.*, 2023
Antidiabetic effects	Almonds can lower glycated haemoglobin levels and improve insulin sensitivity, aiding in diabetes management.	Ojo *et al.*, 2021; Bodnaruc *et al.*, 2020; Gayathri *et al.*, 2023; Madan *et al.*, 2021
Potential anticarcinogenic properties	Certain almond components have shown promise in cancer prevention and therapy through anti-proliferative activities.	Khani and Meshkini, 2020; Ali and Sahib, 2022; Bottone *et al.*, 2020; Oliveira *et al.*, 2020
Effects on weight management and satiety	Almonds may support weight management and enhance feelings of fullness, contributing to dietary satisfaction.	Dreher, 2021; Hollingworth *et al.*, 2019; Ünal and Pekcan, 2020; Brown *et al.*, 2022
Bone health benefits	Almonds are a source of minerals and vitamins essential for bone health, supporting bone structure and strength.	Barreca *et al.*, 2020; Sánchez-Rodríguez *et al.*, 2021; Yee *et al.*, 2021; Mandalari *et al.*, 2023

Researchers also looked at the impact of cultivar and harvest time, concluding that the former enhanced fat content while the latter reduced protein and carbohydrate content. Even across varietals, production years, and growing locales, almonds have the same general nutritional composition (Summo *et al.,* 2018). The researchers discovered no significant changes in the levels of aluminum, iron, calcium, phosphorus, magnesium, zinc, and sodium across almond kernel brands, but there were significant variances in the amounts of proteins, potassium, copper, boron, sulfur, and manganese (Gama *et al.,* 2017). It is advised to consume 30-50 g daily as part of a balanced diet (Gama *et al.,* 2018). Almond water content, lipid content, oil composition, and oil UV absorption coefficients are the main factors that determine almond quality. As a result, much research has assessed the impact of several variables on the quality of almond kernels. Researchers looked at how the beginning and end of August when almonds are harvested affect the fatty acid and mineral concentrations of several types of almonds. An increase in acidity and fat content was seen throughout ripening, with Mas Bovera exhibiting the greatest nutritional value (Piscopo *et al.,* 2010). Subsequent investigations examined the impact of harvest timing and storage circumstances on the two almond cultivars, Texas and Ferragnes. They concluded that, in comparison to late-harvested almonds, early-harvested almonds had more moisture, greater oil quality, and less sugar. They are thus less sweet yet of greater quality (Kazantzis *et al.,* 2003). Almond proteins are known to have a high arginine concentration and excellent digestion (Chen *et al.,* 2006). Researchers also examined the antioxidant activity and total phenolic components of 10 different almond varieties and discovered a significant variation driven by the genetic makeup. Furthermore, the antioxidant activity was found to be higher in late harvest, indicating that the late period of ripening is when antioxidant molecules are most likely to occur (Summo *et al.,* 2018).

6. Allergenic potential

6.1 Prevalence and triggers of almond allergies

Almond allergies, like other nut allergies, are significant due to the potential for severe and life-threatening reactions in sensitive individuals. Almond allergies are part of the tree nut allergy category, known for causing anaphylaxis. The allergenic potential of almonds is associated with several proteins identified as allergens, including but not limited to Pru du 3 (a nonspecific lipid transfer protein), Pru du 4 (profilin), and others which can trigger immune responses in sensitive individuals (Zhang and Jin, 2020; Bezerra *et al.,* 2021). These proteins can remain active even after food processing, maintaining their allergenicity in a wide range of food products. Almond allergens include eight groups of proteins: PR-10, TLP, prolamins, profilins, 60sRP, and cupin, which can trigger mild to life-threatening immune reactions in sensitized individuals (Costa *et al.,* 2012). Pru du 1, an almond Bet v 1 homologue, is a prominent allergen in individuals with almond allergies linked with birch pollen (Kabasser *et al.,* 2022).

6.2 Management of almond allergies and labelling regulations

Management of almond allergies primarily involves avoidance of almonds and products containing almond-derived ingredients. The challenge often lies in identifying these products, as almonds can be found in many processed foods. Individuals with almond allergies must read labels carefully to avoid accidental exposure. In addition to avoidance, those at risk should have an emergency action plan and carry epinephrine auto-injectors to manage potential anaphylactic reactions (Bezerra *et al.,* 2021).

In many countries, food labelling regulations require clear indications of allergens, including tree nuts like almonds, in pre-packaged foods. The European Union's Regulation (EU) No 1169/2011 mandates the labelling of almonds when used as ingredients. However, precautionary allergen labelling (PAL), such as "may contain" statements, remains voluntary and unstandardized, potentially leading to consumer confusion and risk of accidental exposure (Dunn Galvin *et al.,* 2019). Emerging research suggests a need for more standardized approaches to PAL to provide allergic consumers with clearer, more reliable information. Efforts are being made to develop thresholds and standardized testing methods for allergen presence to refine PAL's use and improve safety for allergic individuals (Monaci *et al.,* 2020).

7. Future directions and research needs

While extensive research has been conducted on the nutritional and health benefits of almonds, certain gaps remain, particularly in understanding the mechanistic basis of these benefits and the variability among almond cultivars. For instance, the detailed molecular mechanisms through which almond consumption influences metabolic pathways and reduces the risk of chronic diseases like diabetes and cardiovascular diseases are not fully elucidated. Additionally, there's a need for more comprehensive studies comparing the bioactive compound profiles and health effects of different almond varieties, especially those adapted to various climatic conditions and cultivation practices. Almonds contain a plethora of bioactive compounds with potential health benefits, suggesting a vast area for pharmacological research. For example, the phenolic compounds and antioxidants in almonds have shown promise in reducing inflammation and oxidative stress, indicating potential for the development of natural therapeutic agents. Future research could focus on isolating specific bioactive compounds from almonds and evaluating their efficacy and safety in treating or preventing diseases. Moreover, the role of almond consumption in gut health, particularly its prebiotic effects and impact on the gut microbiome, presents another avenue for pharmacological exploration. Sustainability in almond cultivation and processing is increasingly critical, given the environmental challenges and the need for efficient resource use. These studies collectively suggest that future research should focus on optimizing almond cultivation practices to enhance sustainability. This includes developing drought-resistant cultivars, refining irrigation practices to conserve water, exploring organic and integrated pest management strategies, and improving mechanical harvesting methods to reduce tree damage and improve efficiency (Arroyo *et al.,* 2022; Rijal *et al.,* 2021; Maldera *et al.,* 2021).

8. Conclusion

Almonds, with their rich nutritional and phytochemical composition, offer significant health benefits, including lowering cholesterol levels, improving glycemic control, and reducing the risk of chronic diseases. However, understanding their allergenic potential remains crucial for consumer safety. Future studies should focus on elucidating the molecular mechanisms underlying their health benefits, optimizing sustainable practices, and exploring new therapeutic applications, ensuring almonds continue to contribute to a healthy diet and medicine.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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