Food Frontiers

REVIEW ARTICLE OPEN ACCESS

Recent Advances in the Bioactive Compounds of Prunes (*Prunus domestica* L.) and Their Health Benefits

Luyang Han[1] | Tiantian Fu[1] | Menglin Zhou[1] | Manxi Wu[2] | Han Yang[2] | Jinping Cao[2] | Jinhu Tian[3] | Chongde Sun[2] | Yaqun Liu[4] | Feifei Gao[5] | Yue Wang[2,6]

[1]Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, China | [2]Fruit Science Institute, College of Agriculture and Biotechnology, Zhejiang University, Hangzhou, China | [3]College of Biosystems Engineering and Food Science, National-Local Joint Engineering Laboratory of Intelligent Food Technology and Equipment, Zhejiang Key Laboratory for Agro-Food Processing, Zhejiang Engineering Laboratory of Food Technology and Equipment, Zhejiang University, Hangzhou, China | [4]Department of Bone and Joint Rehabilitation, Qingdao Special Servicemen Recuperation Center of People's Liberation Army Navy, Qingdao, China | [5]School of Food Science and Technology, Shihezi University, Shihezi, Xinjiang, China | [6]Center for Balance Architecture, the Architectural Design & Research Institute of Zhejiang University Co., Ltd., Hangzhou, China

Correspondence: Yaqun Liu (liuyaqun_smmu@163.com) | Feifei Gao (gaofeifei@shzu.edu.cn) | Yue Wang (fruit@zju.edu.cn)

Received: 2 July 2025 | **Revised:** 27 October 2025 | **Accepted:** 8 December 2025

Keywords: antioxidant activity | glycolipid metabolism regulation | immune modulation | laxative effects | osteoporosis prevention | prunes (*Prunus domestica* L.)

ABSTRACT

Prunes (*Prunus domestica* L.) are increasingly recognized for their multifaceted health benefits, which are derived from their rich bioactive compounds. This review aims to consolidate current research on the nutritional components and biological activities of prunes, emphasizing their potential in health promotion and disease prevention. We explore the diverse bioactive compounds in prunes, including polyphenols, polysaccharides, and sorbitol, and their implications for antioxidant, anti-inflammatory, and antimicrobial activities. The review also examines prunes' effects on laxation, osteoporosis prevention, immune modulation, and regulation of glycolipid metabolism. Clinical studies and mechanistic insights are discussed to provide a comprehensive understanding of prunes' health benefits. The review concludes that prunes possess significant health benefits, with future research directions focusing on the identification of active compounds, determination of effective doses, mechanistic research, and clinical validation. This scientific basis for prune-based functional foods and pharmaceuticals development contributes to personalized nutrition strategies, offering a comprehensive overview of prunes' potential in healthcare and disease management.

1 | Introduction

Prunes (*Prunus domestica* L.), a fruit with a long history of cultivation and use, have gained increasing attention in recent years as a prominent functional food due to their remarkable nutritional value and potential health benefits. Originally cultivated in regions around the Caucasus Mountains, between the Black Sea and Caspian Sea, prunes are now widely grown worldwide, including in areas like Ili in Xinjiang, China (Zhebentyayeva et al. 2019). Their global popularity can be attributed to their unique taste and rich nutritional profile but also to a growing body of scientific evidence supporting their diverse bioactive properties. This evidence has solidified their status as a model functional food, capable of delivering health benefits beyond basic nutrition (Wallace 2017).

A growing body of research has highlighted a broad range of health benefits associated with prunes, making them a subject of interest in both nutrition and medicine. Comprehensive reviews have summarized their wide-ranging pharmacological activities, including well-established antioxidant, anti-inflammatory, antimicrobial, and neuroprotective properties (Mishra and Vyas 2021; Shukla and Kishan 2021). Specific benefits that have garnered significant attention include their role in promoting digestive health, partly by positively modulating the gut microbiome (de Souza et al. 2022), preventing bone loss, managing weight, and regulating cholesterol levels (Askarpour et al. 2023; Chey et al. 2021; Navarro-Hoyos et al. 2021; G. Noratto et al. 2015; Park et al. 2023). Prunes are rich in essential vitamins, including vitamins (A, C, and K), minerals (potassium and magnesium), and dietary fiber. They also contain significant amounts of polyphenolic compounds like chlorogenic acid (CGA) and anthocyanins, which are central to their bioactive effects (Stacewicz-Sapuntzakis 2013). These components collectively contribute to prunes' ability to improve various aspects of health.

While individual studies have explored the health-promoting properties of prunes, several reviews have also summarized their general phytochemical and pharmacological activities (Mishra and Vyas 2021; Shukla and Kishan 2021). These works have laid a valuable foundation by documenting the broad therapeutic potential of *Prunus domestica*. However, there remains a need for an updated and focused synthesis that delves deeper into the recent mechanistic insights and consolidates the growing body of clinical evidence. Much of the existing research on mechanisms is fragmented across specific health outcomes, such as osteoporosis, gut health, and metabolic regulation. Therefore, this review aims to build upon previous work by systematically analyzing the latest research on the nutritional components and biological activities of prunes. We will place a strong emphasis on elucidating the molecular mechanisms of action underlying their health benefits and assessing their therapeutic applications based on recent clinical trials. While other species in the genus, such as *Prunus spinosa*, also exhibit notable health benefits (Bei et al. 2024), our focus remains strictly on *Prunus domestica* L. By synthesizing these advanced findings, this review will not only contribute to the understanding of prunes' health benefits but also provide a scientific basis for the development of functional foods and drugs based on prunes.

2 | Bioactive Compounds of Prunes

2.1 | Polyphenols

Polyphenols are the primary bioactive compounds in prunes and are widely recognized for their health-promoting effects. These compounds, abundant in many fruits, contribute to a variety of biological activities, including antioxidant activity, osteoporosis inhibition, anti-inflammatory effects, obesity prevention, regulation of glucose metabolism, and modulation of gut microbiota and cholesterol metabolism (Drogoudi and Pantelidis 2022; Navarro-Hoyos et al. 2021; Navarro et al. 2018; Smith et al. 2022; Mirza et al. 2018; G. Noratto et al. 2015; Rybak and Wojdylo 2023; Chiu et al. 2017).

The polyphenols in prunes can be categorized into four major groups: phenolic acids, flavonols, anthocyanins, and flavan-3-ols. It is noteworthy that while some classifications define polyphenols strictly as compounds with multiple phenolic rings, the term is broadly used in nutrition and food science to include major groups of phenolic compounds like phenolic acids, which are structurally diverse (Manach et al. 2004). Each of these groups has distinct health benefits, contributing to the overall bioactivity of prunes (Figure 1).

2.1.1 | Phenolic Acids

Phenolic acids are a predominant class of polyphenols in prunes, broadly categorized into hydroxybenzoic acids and hydroxycinnamic acids. This group includes hydroxybenzoic acids such as syringic acid, protocatechuic acid, and gallic acid, as well as derivatives of hydroxycinnamic acid, most notably CGA, neochlorogenic acid, and caffeoylshikimic acid (Michalska, Wojdylo, Lech, et al. 2016; Michalska, Wojdylo, Majerska, et al. 2019; Miletić et al. 2013).

Neochlorogenic acid and CGA are the most abundant phenolic acids in prunes. These compounds are renowned for their potent antioxidant and anti-inflammatory properties, which they exert by effectively neutralizing free radicals and inhibiting the production of proinflammatory cytokines such as TNF-α and IL-6, primarily through the modulation of the NF-κB signaling pathway (Navarro-Hoyos et al. 2021; Santana-Gálvez et al. 2017). Moreover, CGA has been strongly implicated in the regulation of glucose metabolism. It can improve insulin sensitivity and lower postprandial blood glucose levels by inhibiting enzymes like α-glucosidase and glucose-6-phosphatase, making it beneficial for managing hyperglycemia (Rybak and Wojdyło 2023; Tajik et al. 2017). Other phenolic acids, while present in smaller quantities, also contribute to the overall bioactivity, with protocatechuic acid demonstrating significant radical-scavenging and antimicrobial activities (Kakkar and Bais 2014).

2.1.2 | Flavonols

Flavonols are derivatives of quercetin, kaempferol, and myricetin, often present as monosaccharides or disaccharides, with rutin being the most common flavonols in prunes (Michalska, Wojdylo, Lech, et al. 2016; Michalska, Wojdylo, Majerska, et al. 2019; Tomic et al. 2019). These flavonol compounds are commonly found in the *Rosaceae* family and are similar to those found in apples and peaches (Navarro et al. 2018; G. Noratto et al. 2015). Flavonols contribute to prunes' antioxidant and anti-inflammatory effects by modulating oxidative stress and inflammation pathways. They also play a role in the prevention of bone loss, potentially through the inhibition of osteoclast differentiation (Smith et al. 2022).

2.1.3 | Anthocyanins

Anthocyanins, the coloring agents in prunes, consist of cyanidin and peonidin aglycones, with glycosides including glucoside, xyloside, and rutinoside. Among these, cyanidin-3-*O*-glucoside and cyanidin-3-*O*-rutinoside are the most abundant, which are responsible for their purple color (Michalska, Wojdylo, Lech, et al. 2016; Michalska, Wojdylo, Majerska, et al. 2019; Sahamishirazi et al. 2017; Tomic et al. 2019; Wesche-Ebeling 1996). These

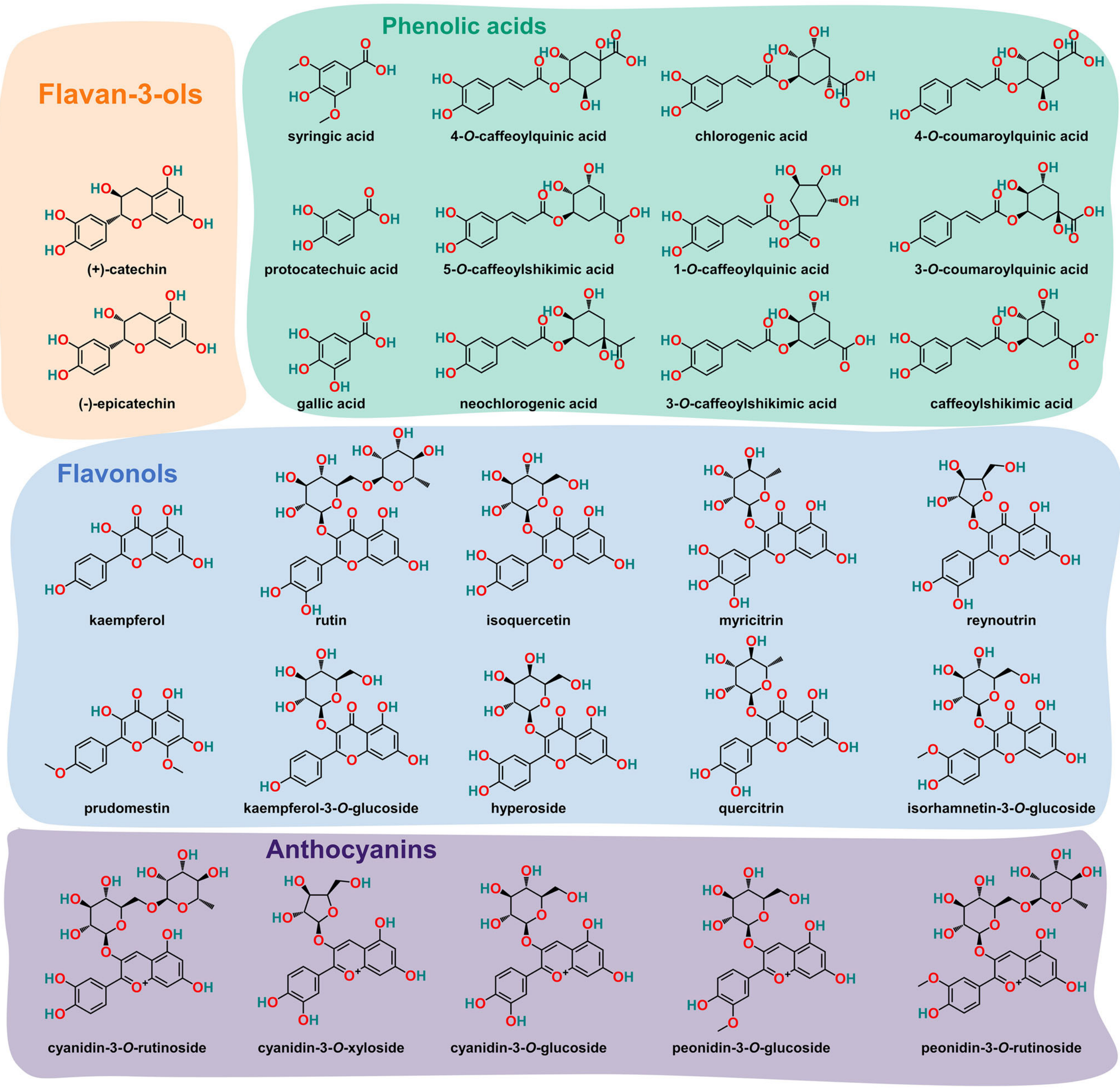

FIGURE 1 | Classification of major polyphenolic compounds in prunes.

compounds have strong antioxidant effects, protecting cells from oxidative damage (Navarro et al. 2018).

2.1.4 | Flavan-3-ols

Flavan-3-ols are predominantly represented by catechin and epicatechin (Michalska, Wojdylo, Lech, et al. 2016). Flavan-3-ols are known for their potent antioxidant properties and their ability to inhibit the activities of enzymes involved in oxidative stress (Kimura et al. 2008; Navarro et al. 2018).

The polyphenol content in prunes is influenced by several factors, including fruit variety, tissue type, maturity, harvest timing, environmental conditions (such as temperature, light, and moisture), and processing methods like drying (Michalska, Wojdylo, Majerska, et al. 2019; Sahamishirazi et al. 2017; Tomic et al. 2019; Wesche-Ebeling et al. 1996). For example, while the combination of convective predrying and microwave finish-drying may better preserve polyphenols compared to vacuum drying, the exact impact of different drying methods on the bioavailability of polyphenols in prunes requires further investigation (Michalska, Honke, et al. 2016).

2.2 | Polysaccharides

The polysaccharides in prunes are primarily concentrated in the cell wall, with pectin and hemicellulose being the major components. Pectin is one of the most important polysaccharides, characterized by a high content of uronic acids and a relatively low content of cellulose glucose (Renard and Ginies 2009). The high degree of methylation in pectin may affect its gelling properties and solubility during food processing (Renard and Ginies 2009). The main component of hemicellulose is glucuronoxylan, which contains xylose, glucose, galactose, and small amounts of fucose (Renard and Ginies 2009). The neutral sugars in the cell wall of prunes are mainly galactose and arabinose, and their proportions vary among different cultivars (Renard and Ginies 2009). Prune pectin polysaccharides have a complex branched structure, where glucose may be directly linked to galacturonic acid (GalA) either as single residues or in the form of cellobiose (Nunes et al. 2012). The dietary fiber content in prune pomace is five to nine times higher than that in the flesh, indicating that pomace is a rich source of dietary fiber (Kosmala et al. 2013). The physical properties of prune polysaccharides, such as water-holding capacity and swelling ability, are also influenced by their composition and structure (Kosmala et al. 2013). Popov et al. extracted pectin polysaccharides (PD) from prunes and discovered a complex structure, with the linear regions are mainly composed of GalA and rhamnogalacturonan (RG), while the branched regions primarily consist of 1,4-linked β-D-galactopyranose residues, along with a smaller amount of 1,5-linked α-L-arabinofuranose residues (Popov et al. 2014).

The composition and structure of prune cell wall polysaccharides are affected by variety, ripeness, and processing methods. There are significant differences in the polysaccharide composition of the cell wall among different prune varieties, and changes in ripeness may alter the composition and structure of the polysaccharides, influencing their behavior during processing (Renard and Ginies 2009). Furthermore, processing methods, such as enzyme-assisted extraction, can significantly impact the extraction efficiency and functionality of polysaccharides (Fatimi et al. 2007; Kosmala et al. 2013). The degradation of prune polysaccharides and fruit softening are closely related to the activity of cell wall-degrading enzymes. Studies have shown that 1-methylcyclopropene (1-MCP) treatment could significantly inhibit the activity of these enzymes, reducing polysaccharide degradation and thus delaying fruit softening (Lin et al. 2018). In addition, different extraction methods significantly affect polysaccharide yield and quality. Extraction using simulated gastric fluid yields a higher output with better bioactivity (Popov et al. 2014), while using weak organic acids such as citric acid is environmentally friendly and may retain more bioactive compounds (Konrade et al. 2023). Cantu-Jungles et al. successfully isolated polysaccharides with different structural characteristics from prunes through various extraction and purification steps, showing notable gastroprotective effects (Cantu-Jungles et al. 2014).

In terms of bioactivity, prune polysaccharides exhibit notable anti-inflammatory and antioxidant properties. Studies have shown that these polysaccharides possess anti-inflammatory and antioxidant activities, capable of inhibiting the production of superoxide anion radicals, reducing the adhesion of inflammatory cells, and possibly exerting their effects by modulating cellular signaling pathways (Popov et al. 2014). These polysaccharides offer various health benefits, such as significantly reducing the expression of inflammatory markers, including nitric oxide (NO) and cyclooxygenase-2 (COX-2), induced by lipopolysaccharides (LPS) in RAW 264.7 macrophages (Nunes et al. 2012). Therefore, research on prune polysaccharides not only contributes to understanding their roles in food processing and nutritional health but also holds potential for providing valuable raw materials for the pharmaceutical and cosmetic industries.

Pectin and hemicellulose, as the principal polysaccharides in prunes, exhibit distinct differences in their core structure and monosaccharide composition, leading to diverse biological functions and nutritional significance (Figure 2).

2.3 | Sorbitol

Sorbitol is a key nonstructural carbohydrate in prunes, contributing to their natural sweetness and taste (Cinquanta et al. 2002). Both prunes and prune juice contain relatively high levels of sorbitol, which not only influences their sensory properties but also plays a significant role in the health benefits attributed to these fruits (Gill et al. 2019; Stacewicz-Sapuntzakis 2013). The sorbitol content in prunes is influenced by factors such as cultivar, ripeness, and processing methods. For example, dehydration and heating during processing can alter sorbitol levels. The analysis of dried prunes from major producing countries (United States, Chile, France, and Argentina) showed a high sorbitol content, ranging from 11.2 g/100 g to 15.5 g/100 g, which is notably higher than the content in their nondried counterpart plums (5.4 g/100 g; Gill et al. 2019; Stacewicz-Sapuntzakis et al. 2001). Climate conditions, especially precipitation and temperature, have a significant impact on sorbitol content. Under water stress, the accumulation of sorbitol may be related to changes in enzyme activity. Indeed, sorbitol exhibited a significant negative correlation with precipitation ($r = -0.222$) and a significant positive correlation with temperature ($r = 0.472$). This correlation suggests that, compared to the relatively wetter period of 2008–2011, the accumulation of sorbitol in plum fruits reached its maximum annual average content of 4.06% in the water-deficit and high-temperature conditions observed in 2012 (Dugalic et al. 2014). Organic farming systems, which often expose plants to controlled stress, tend to result in higher sorbitol content, potentially due to the enhanced accumulation of secondary metabolites (Usenik 2021). Additionally, the sorbitol content varies among different prune cultivars and remains relatively stable during drying, suggesting that physical pretreatments such as peeling or soaking do not significantly affect sorbitol levels (Cinquanta et al. 2002).

Sorbitol has a laxative effect, which may help prevent constipation and be beneficial for gut health by promoting the growth of beneficial bacteria, thus acting as a prebiotic (Gill et al. 2019; Stacewicz-Sapuntzakis 2013). Sorbitol is metabolized more slowly than glucose, and a significant portion may reach the intestines, where microbial fermentation could result in bloating and loose stools (Stacewicz-Sapuntzakis et al. 2001). Sorbitol could significantly inhibit intestinal glucose absorption in diabetic rats, increase glucose utilization in muscle tissue, and lower blood glucose levels (Niu et al. 2024). This suggests potential benefits for dietary management in diabetic patients (Gill et al. 2019). Sorbitol may also influence calcium absorption; studies have shown that certain sugars can enhance calcium absorption in the intestines of rats, and sorbitol may act through a similar mechanism (Stacewicz-Sapuntzakis 2013).

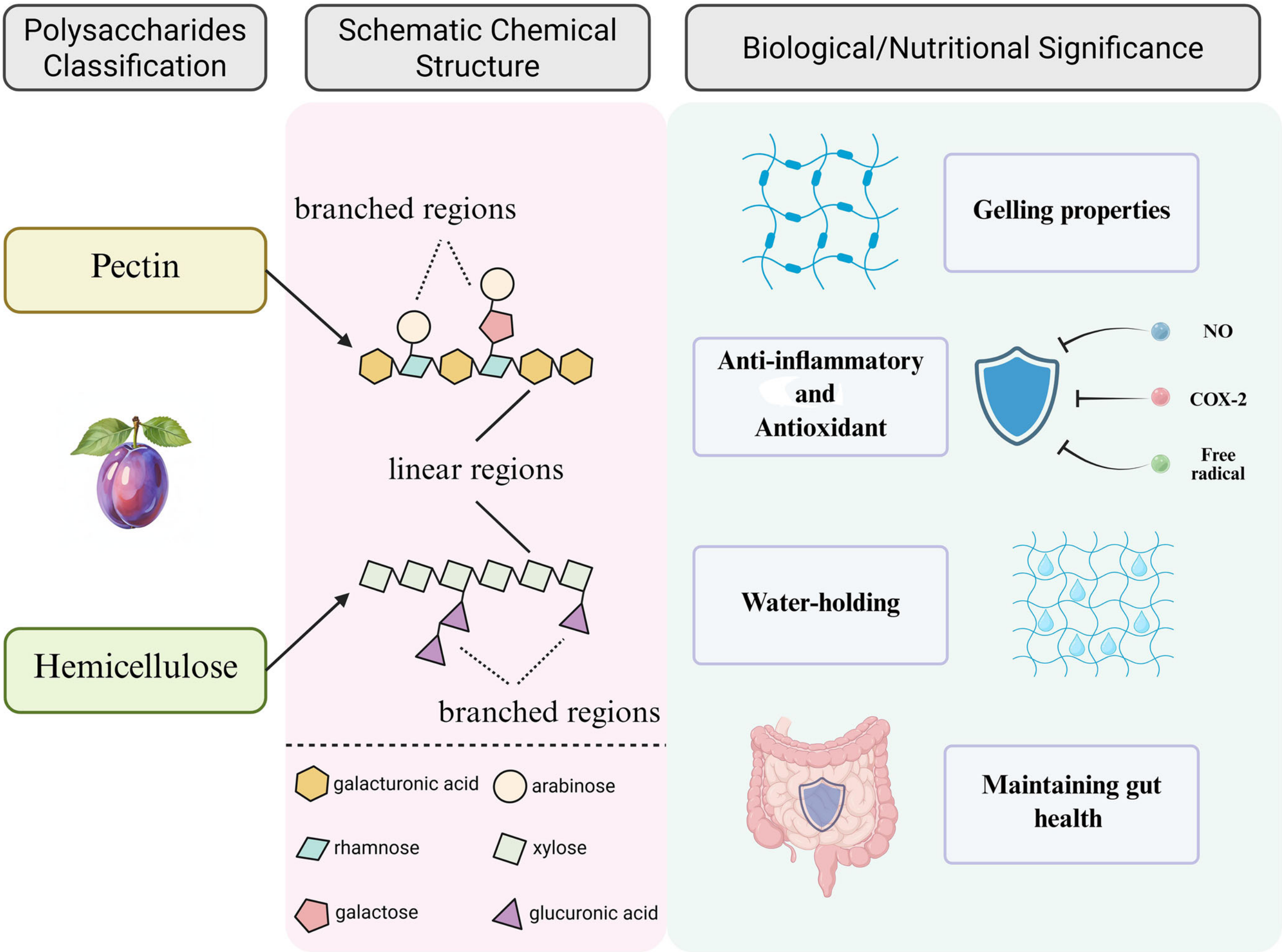

FIGURE 2 | Major polysaccharides in prunes.

2.4 | Other Bioactive Compounds

In addition to polyphenols, polysaccharides, and sorbitol, prunes and their by-products, particularly the kernels, contain other bioactive molecules such as fatty acids and proteins.

2.4.1 | Fatty Acids

While the flesh of the prune is characteristically low in fat, the kernel is a rich source of fixed oil. Prune kernel oil is predominantly composed of unsaturated fatty acids, with oleic acid (a monounsaturated omega-9) and linoleic acid (a polyunsaturated omega-6) being the most abundant (Savic et al. 2020). These fatty acids are known for their beneficial effects on cardiovascular health, helping to lower LDL cholesterol levels and exerting anti-inflammatory properties (Saini and Keum 2018).

2.4.2 | Proteins and Bioactive Peptides

Similar to lipids, the protein content in prune flesh is minimal. However, prune seeds contain a significant amount of protein that can serve as a source of bioactive peptides. Recent in silico studies have identified several peptides, including HLLP, LPLL, LPAGV, and NLPL, derived from prune seed proteins (Gupta et al. 2024). These peptides are predicted to have potent immunomodulatory activity by inhibiting proinflammatory cytokines IL-17A and IL-23, suggesting their potential as therapeutic agents for autoimmune diseases like systemic lupus erythematosus (SLE). While promising, this research is still in a preliminary stage and requires further experimental validation to confirm these health benefits. The valorization of prune kernels for protein and peptide extraction represents a promising avenue for utilizing food industry by-products (Udenigwe and Aluko 2011).

3 | Health Benefits of Prunes

3.1 | Laxative Effects

Constipation is a common gastrointestinal disorder characterized by infrequent bowel movements, hard stools, and difficulty in defecation. It is often caused by factors such as poor dietary habits, lack of physical activity, psychological stress, certain medications, and chronic diseases (Hull et al. 1980). Populations such as older adults, pregnant women, bedridden individuals, and those with chronic conditions are particularly susceptible to constipation (Higgins and Johanson 2004).

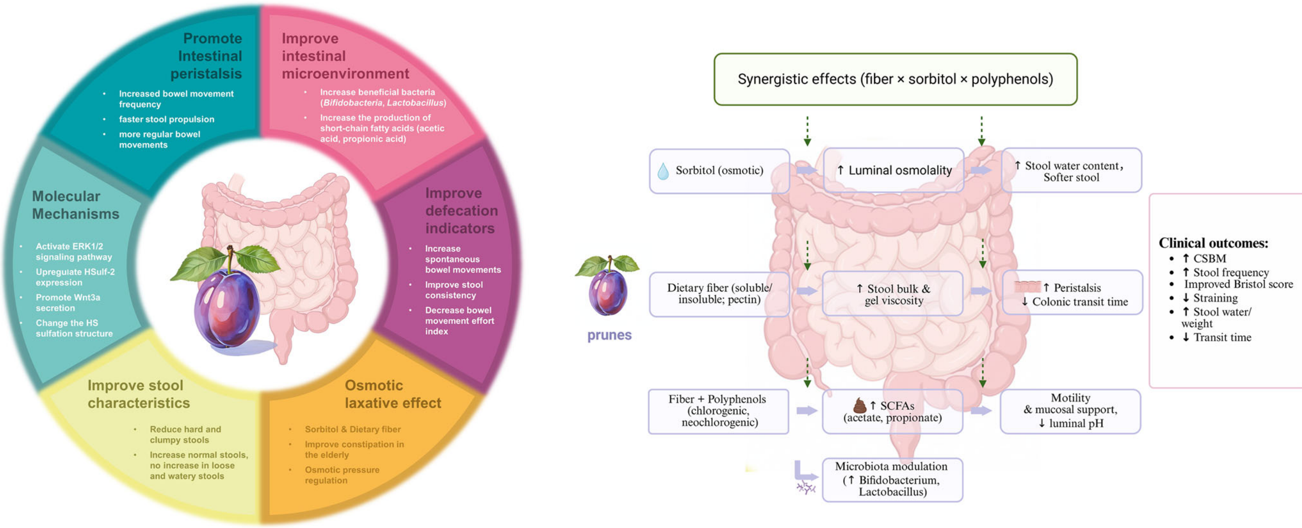

FIGURE 3 | Laxative effects of prunes.

Beyond causing direct physiological complications such as hemorrhoids, anal fissures, and intestinal obstruction, constipation can also lead to psychological issues like anxiety and depression (Cheng et al. 2003), significantly affecting quality of life. In some cases, chronic constipation may indicate underlying health problems such as colorectal cancer or other gastrointestinal conditions (Watanabe et al. 2004). Effective prevention and treatment strategies are therefore crucial, and lifestyle changes—such as increased fiber intake, proper hydration, and regular physical activity—are foundational in managing this condition. Natural interventions, such as consuming prunes, have been shown to significantly alleviate constipation, likely due to their high-fiber and sorbitol content (Chey et al. 2021; Chiu et al. 2017).

Prunes are widely recognized for their laxative properties, which are one of their most well-established health benefits. The exact mechanisms responsible for their laxative effects remain an area of active investigation, but studies consistently show that prunes can effectively relieve constipation, improve stool consistency, and enhance bowel motility (Figure 3).

3.1.1 | Laxative Phenotype

Although the exact active components responsible for the laxative effects of prunes remain unclear, numerous studies, particularly clinical trials, have consistently demonstrated the efficacy of prunes in relieving constipation. These findings suggest that prunes may have multiple mechanisms of action, which can complement each other in promoting bowel regularity. For example, Lever et al. conducted a randomized controlled trial (RCT) and found that prune consumption significantly increased stool weight and frequency. They proposed that this effect could be attributed to prunes' ability to enhance intestinal motility by increasing both the volume and water content of intestinal contents. In line with this, prunes may also promote gut health by modulating gut microbiota composition and stimulating the production of short-chain fatty acids (SCFAs), which further support gastrointestinal function (Lever et al. 2019). In a similar vein, Hull et al. demonstrated that a combination of prune juice and bran was effective in improving constipation among older adults. This outcome was primarily attributed to the synergistic effects of prunes' dietary fiber and sorbitol, an osmotic laxative, which together help soften stools and increase stool frequency (Hull et al. 1980). Furthermore, Chey et al. showed that daily consumption of 100 g of prunes for 4 weeks significantly increased the frequency of complete spontaneous bowel movements (CSBMs), improved stool consistency, and reduced straining in adults with chronic constipation. This suggests that prunes not only enhance stool frequency but also improve stool quality, reducing discomfort during bowel movements (Chey et al. 2021).

Koyama et al.'s 8-week prune juice intervention supports these findings, demonstrating that prunes can reduce the occurrence of hard and lumpy stools while promoting normal stool consistency, without causing diarrhea or loose stools. The absence of adverse events or side effects in their study underscores the safety profile of prunes as a long-term solution for constipation (Koyama et al. 2022). These results align with those of Attaluri et al., who compared prunes to psyllium, a commonly used fiber supplement. Despite both providing the same amount of fiber (6 g/day), prunes were more effective at increasing weekly CSBMs and improving stool consistency. This suggests that the laxative effect of prunes might involve more than just fiber content, potentially pointing to the additional roles of sorbitol and bioactive compounds like phenolic acids in promoting bowel regularity (Attaluri et al. 2011).

In elderly volunteers with constipation, Sairanen et al. explored a combined intervention of prunes (12 g/day), galacto-oligosaccharides (GOS, 12 g/day), and flaxseeds (6 g/day) in elderly participants. This combination significantly softened stools and alleviated constipation. The contribution of prunes to this effect can be attributed not only to their high-fiber and sorbitol content but also to their phenolic compounds, such as neochlorogenic acid and CGA, which may enhance their stool-softening properties. This further illustrates how prunes' multiple bioactive components may work synergistically to improve gut function (Sairanen et al. 2007).

3.1.2 | Gut Microbiome and Additional Mechanisms

The gut plays a central role in mediating the bioactive effects of prunes, enabling them to regulate cholesterol, improve obesity outcomes, and support bone health. Chiu et al., in a randomized, placebo-controlled study, demonstrated that a 4-week intervention with prune extract concentrate (PEC) significantly increased beneficial gut bacteria, such as *Bifidobacterium* spp. and *Lactobacillus* spp., while reducing harmful bacteria, including *Clostridium perfringens* and *Escherichia coli*, in participants with mild hypercholesterolemia. These changes were accompanied by significant reductions in total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-c), suggesting that prunes may promote cholesterol regulation via gut health modulation (Chiu et al. 2017). Similarly, Noratto et al. found that sugar-free prune juice altered the gut microbiome composition in obese Zucker rats, increasing the abundance of *Bacteroidetes*, *Faecalibacterium*, and *Lactobacillus*. The intervention also elevated fecal concentrations of SCFAs, such as acetate and propionate, which are products of microbial fiber fermentation. Additionally, rats consuming prune juice exhibited lower body weight compared to those fed with peaches, highlighting the dual effects of prunes on both gut health and obesity (G. D. Noratto et al. 2014). In a 12-month RCT, Simpson et al. explored the impact of prunes on the gut microbiome in postmenopausal women. The study found that prunes improved gastric motility, supported cardiovascular health, and helped mitigate bone loss. Furthermore, changes in the gut microbiome were correlated with alterations in urinary phenolic metabolites and plasma inflammatory markers, such as IL-1β, suggesting potential mechanisms underlying these health benefits (Simpson et al. 2022).

3.1.3 | Mechanisms of Laxative Action

The molecular mechanisms underlying the laxative effects of prunes remain incompletely understood, with current studies still in the preliminary stages. Nishida et al. investigated the role of pectin from *Prunus domestica* in modulating intestinal epithelial function. They found that prune pectin interacts with fibronectin and binds to the $\alpha5\beta1$ integrin, thereby activating the ERK1/2 signaling pathway. This activation led to increased expression of heparan sulfate 6-*O*-endosulfatase 2 (HSulf-2), which modified the sulfation patterns of heparan sulfate (HS), a glycosaminoglycan involved in cell signaling, on the surface of differentiated Caco-2 cells (Nishida et al. 2014). In follow-up studies using Caco-2 and rat IEC-6 cell models of the intestinal epithelium, the same group showed that prune pectin further altered HS structures on Caco-2 cells and enhanced the secretion of Wnt3a. This secretion indirectly stimulated the proliferation of IEC-6 cells (Nishida, Murata, Oshima, et al. 2015). The authors hypothesized that these alterations in HS structure and Wnt3a signaling might mediate the morphological changes in the small intestine induced by prune pectin, which could contribute to the laxative effects of prunes.

3.2 | Osteoporosis Prevention Effects

Osteoporosis is a progressive bone disease characterized by a decrease in bone mineral density (BMD) and structural deterioration, which increases fracture risk. It is a major concern in aging populations, especially postmenopausal women, where hormonal changes contribute to bone loss (Damani et al. 2022). Risk factors include not only aging and gender but also lifestyle factors such as lack of physical activity, poor nutrition (e.g., insufficient calcium and vitamin D), smoking, and excessive alcohol consumption (Zhu and Prince 2015). Medications like glucocorticoids, which affect bone metabolism, and other chronic conditions also exacerbate osteoporosis risk (Banu 2013). The disease can lead to severe health consequences, including fractures, chronic pain, immobility, and a reduced quality of life. Therefore, effective prevention strategies are critical for reducing the burden of osteoporosis, with emerging natural products, such as prunes, showing promising potential.

Prunes are rich in bioactive compounds, including boron, magnesium, potassium, and polyphenolic compounds, which are believed to play crucial roles in supporting bone metabolism. These bioactive compounds may inhibit bone resorption and stimulate bone formation, positioning prunes as an effective dietary strategy for osteoporosis prevention (Damani et al. 2022; George et al. 2022). Beyond their rich nutrient profile, prunes offer unique molecular mechanisms that affect osteoblast and osteoclast activity, providing a holistic approach to managing osteoporosis (Figure 4).

3.2.1 | Effects of Prunes in Regulating Osteoblast Activity

Prunes contain a variety of bioactive compounds, including polyphenols, carbohydrates, and nanovesicles, which have shown promising effects in regulating osteoblast activity. Park et al. identified that exosome-like nanovesicles derived from prunes (PENVs) significantly promoted the proliferation, differentiation, and mineralization of MC3T3-E1 preosteoblast cells through the BMP-2/MAPK/Smad1-dependent Runx2 signaling pathway. This process upregulated the expression of key osteoblast differentiation genes and proteins. The findings suggest that prune-derived nanovesicles play a crucial role in enhancing bone formation by stimulating osteoblast activity, providing a potential strategy for osteoporosis management (Park et al. 2023). Graef et al. analyzed prune polyphenol extracts and identified two active fractions, DP-FrA and DP-FrB, which significantly enhanced bone morphogenetic protein (BMP) signaling. These fractions increased the expression of *Bmp2* and *Runx2* genes and elevated the phosphorylation levels of Smad1/5 proteins. Consequently, extracellular alkaline phosphatase (ALP) activity and mineralized nodule formation in MC3T3-E1 cells were enhanced. Notably, DP-FrB upregulated Tak1 and Smad1 expression while increasing phosphorylated p38 protein levels. In primary osteoblasts, both DP-FrA and DP-FrB reversed TNF-α-induced ALP activity suppression, further promoting mineralization and osteoblast function (Graef et al. 2018). Similarly, Delgado Cuenca et al. further explored the effects of prune consumption on human osteoblast activity and gene expression. Their study revealed that prune-derived polyphenolic compounds increased ALP activity and upregulated critical bone marker genes, including RUNX2, osterix, β-catenin, and CX43, thus enhancing osteoblast function and bone formation (Delgado Cuenca et al. 2017).

An intriguing study by Léotoing et al. investigated the effects of prune extracts with differing CGA content on femoral BMD in

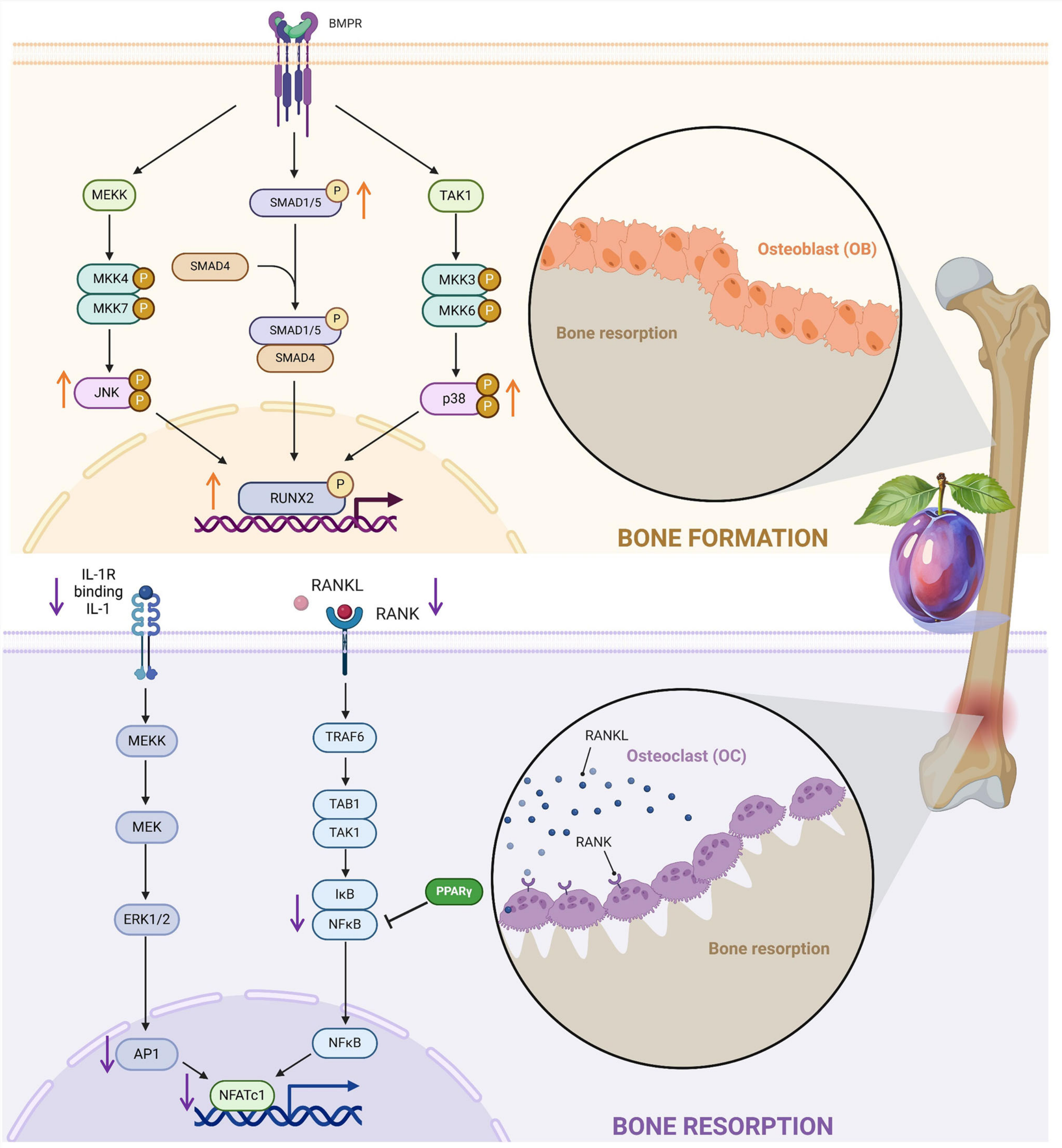

FIGURE 4 | Osteoporosis prevention effects of prunes.

ovariectomized rats, a model for postmenopausal osteoporosis. The researchers compared high-chlorogenic acid (HCA) and low-chlorogenic acid (LCA) prune extracts and found that a high-fiber diet supplemented with LCA prune juice concentrate effectively prevented the reduction in total femoral BMD caused by estrogen deficiency. Interestingly, the findings suggest that the bone-protective effects of prunes may not be entirely dependent on their polyphenol (CGA) content. This raises the possibility that other bioactive components in prunes, such as dietary fiber or specific micronutrients, may contribute significantly to their beneficial effects on bone health. These results highlight the need for further research to identify and understand the mechanisms of these additional components, which could broaden the therapeutic potential of prunes in osteoporosis management (Leotoing et al. 2016).

3.2.2 | Prunes' Role in Modulating Osteoclast Activity and Inflammation

In addition to promoting osteoblast function, prunes also influence osteoclast activity, thereby balancing bone resorption and formation. Shahnazari et al. found that prune supplementation reduced osteoclast surface and serum CTX levels, key markers of bone resorption, in C57Bl/6 mice. This was accompanied by a reduction in proinflammatory cytokines, such as IL-1, TNF, and MCP-1, suggesting that prunes may have anti-inflammatory effects that support bone health (Shahnazari et al. 2016). In a subsequent study, Smith et al. demonstrated that prune polyphenols suppressed osteoclast differentiation through NFATc1 inhibition, while simultaneously restoring osteoblast activity via BMP-2 signaling. These findings highlight prunes' dual role in regulating both osteoblast and osteoclast activity, contributing to bone health through a balance of bone formation and resorption (Smith et al. 2022). In another study, Deyhim et al. evaluated the restorative effects of prunes on bone density in a postmenopausal osteoporosis model using ovariectomized rats. They demonstrated that prune supplementation significantly restored bone density in the femur and tibia, improved lumbar vertebrae bone density, and enhanced the overall mechanical strength of bones, including yield strength and ultimate strength. Furthermore, prunes improved trabecular microstructural properties, contributing to an overall increase in bone quality (Deyhim et al. 2005).

In clinical research, Damani et al. comprehensively reviewed the benefits of prunes for postmenopausal women with osteoporosis. A daily intake of 50–100 g of prunes over 6–12 months was consistently associated with improved bone health, highlighting their potential as a natural dietary intervention. The underlying mechanisms are thought to involve antioxidative and anti-inflammatory pathways, including the inhibition of NF-κB and NFATc1 signaling. This reduces cytokine expression in osteoclast precursors and suppresses TNF-α secretion by monocytes and T cells. Additionally, prunes may mitigate oxidative stress and influence gut microbiota composition, thereby modulating immune responses and maintaining gut barrier integrity—both of which are critical for bone health (Damani et al. 2022). George et al. investigated the effects of prunes on bone metabolism in male patients with osteoporosis. A daily intake of 50 g of prunes for 3 months significantly reduced serum osteocalcin and osteoprotegerin (OPG) levels while increasing the OPG:RANKL ratio, suggesting a beneficial effect on bone turnover (George et al. 2022). Al-Dashti et al., through a randomized crossover trial, examined the short-term impact of prune consumption on bone resorption in healthy postmenopausal women. They observed a notable decrease in serum C-terminal telopeptide of type I collagen (CTX), a marker of bone resorption, indicating that prunes might help reduce bone loss even in the short term (Al-Dashti et al. 2019). Hooshmand et al. conducted several studies using dual-energy X-ray absorptiometry (DEXA) to measure BMD in postmenopausal women with osteoporosis. Their results showed that prunes prevent bone loss by suppressing bone resorption (reducing TRAP-5b levels) and promoting bone formation (elevating the BAP/TRAP-5b ratio; Hooshmand, Chai, et al. 2011; Hooshmand, Kern, et al. 2016). In parallel, their research on healthy males found that prune consumption reduced bone resorption markers (CTX and TRAP-5b), likely through mechanisms involving IGF-I signaling. These findings support the hypothesis that prunes improve bone health by simultaneously promoting bone formation and inhibiting bone resorption (Hooshmand, Gaffen, et al. 2022).

3.2.3 | Prune Supplementation in Special Conditions: Radiation, Microgravity, and Maternal Effects

Prunes have also shown potential in specialized applications, such as preventing bone loss caused by radiation and microgravity. Schreurs et al. demonstrated that prune powder effectively suppressed radiation-induced upregulation of osteoclastogenesis-related genes, including *Rankl*, *Mcp1*, and *Tnf-α*, which are associated with bone loss due to oxidative stress. This suggests that prunes may offer a protective role in radiation-associated bone degeneration (Schreurs et al. 2016). Similarly, Steczina et al. found that prune supplementation preserved bone microstructure and mechanical properties in mice subjected to simulated spaceflight conditions, which is important for bone health in astronauts (Steczina et al. 2020). Additionally, Monsefi et al. showed that maternal prune supplementation during pregnancy enhanced offspring bone development, suggesting that prunes may influence bone health across generations (Monsefi et al. 2013). These studies underscore the broad potential of prunes in both specialized and everyday bone health applications.

3.3 | Immune Modulation Effects

Immune-related diseases, including autoimmune diseases and immunodeficiency disorders, result from dysfunctions in the immune system. Autoimmune diseases, such as SLE and rheumatoid arthritis (RA), occur when the immune system erroneously targets the body's own tissues, leading to chronic inflammation and progressive tissue damage (Alarcon-Segovia et al. 2005). In contrast, immunodeficiency disorders, exemplified by acquired immunodeficiency syndrome (AIDS), are characterized by impaired or deficient immune function, rendering individuals more susceptible to infections and other complications (Chinen and Shearer 2010). The etiology of these diseases is multifactorial, involving genetic predisposition, environmental factors (e.g., viral infections, specific medications, ultraviolet radiation, or exposure to radiation), and aberrant immune cell functionality (Basso et al. 2014). Additionally, dietary components, such as high-sugar intake, gluten, and dairy products, are considered potential environmental triggers that may exacerbate immune dysregulation in susceptible individuals (Mirza et al. 2018; Popov et al. 2014). The clinical manifestations of immune diseases are diverse and can include chronic inflammation, tissue destruction, and organ dysfunction, often resulting in debilitating symptoms such as pain, joint deformities, and fatigue (Gupta et al. 2024; Karasawa et al. 2012; Youssef, Menze, et al. 2020). Emerging evidence suggests that dietary interventions may play a pivotal role in modulating immune responses, potentially mitigating the severity or progression of immune-related diseases (Table 1; Limketkai et al. 2023; Okawa et al. 2020; Xiao et al. 2024).

3.3.1 | Prunes Contribute to Immune Regulation by Modulating

Prunes exhibit significant anti-inflammatory properties through multiple mechanisms and bioactive components. Popov et al. demonstrated that prune polysaccharides significantly inhibit PMA-induced adhesion of peritoneal leukocytes, particularly

TABLE 1 | The modulating effect of prune on immunity.

Prune materials	Immune problem	Model	Improvement	Mechanism	References
Pectic polysaccharides	Inflammation	PMA induced leukocyte adhesion assay	Leukocyte adhesion ↓	\	Popov et al. (2014)
Fruit	Inflammatory arthritis	TNF transgenic mice, human synovial fibroblasts, mouse bone marrow macrophages	Onset of arthritis ↓ Osteoclastogenesis ↓ Bone erosions ↓ synovitis ↓ Protection of articular cartilage	IL-1β ↓ MCP1 ↓ MIP1α ↓ MMP1 & 3 ↓ RANKL ↓ NFATc1 ↓	Mirza et al. (2018)
Polyphenols	Inflammation	LPS induced inflammation in RAW264.7 cell line	NO ↓ COX-2 ↓	\	Hooshmand et al. (2015)
Prune extracts	Allergic	BALB/c mice sensitized by intraperitoneal injection of mite antigen and aluminum adjuvant	Sneezing events ↓ mite-specific IgE in serum ↓ the ratio of IFN-γ^+CD4$^+$ cells to IL-4$^+$CD4$^+$ cells ↑	*Btk* ↓ *Stim1* ↓	Karasawa et al. (2012)
Peptides	Systemic lupus erythematosus	In silico drug likeliness and ADMET prediction, molecular docking	Inhibition of IL-17A and IL-23	\	Gupta et al. (2024)
Prune gum-stabilized nanoparticles	Inflammation	Carrageenan-induced paw edema	Mouse paw edema ↓	\	Islam et al. (2017)
Fruit	Inflammation	LPS, TNF-α, and IL-1β induced inflammation in Caco-2 cell line and Caco-2/HT-29-MTX/THP-1 coculture system	IL-6 ↓ IL-8 ↓	*Nrf2* ↓ *MAPK14* ↓ *NF-κB* ↓	Kaulmann et al. (2016)
Juice	Inflammation	LPS induced inflammation in RAW264.7 cell line	NO ↓	\	Silvan et al. (2020)
Lignan	Inflammation	Lithium/pilocarpine-induced epileptic seizures in Wistar rats	Seizures onset ↓ Seizures duration ↓ Seizures score ↓	COX-2 ↓ iNOS ↓ strong binding affinity with of 5-LOX	Youssef, Menze, et al. (2020)

after digestion with 1,4-α-D-polygalacturonase, which targets the PD-1 component (Popov et al. 2014). Similarly, Hooshmand et al. observed that 1000 µg/mL of prune polyphenols reduced NO production by 43% and MDA by 32% in LPS-induced RAW264.7 cells. They also significantly inhibited COX-2 expression, further confirming the anti-inflammatory potential of prune polyphenols (Hooshmand et al. 2015). Silvan et al. corroborated these findings, reporting that prune juice extracts suppress LPS-induced NO production (Silvan et al. 2020). Furthermore, Kaulmann et al. showed that prune extracts reduce IL-6 secretion in THP-1 cells and IL-8 levels in intestinal cell coculture models, highlighting their positive impact on gut-related inflammation (Kaulmann et al. 2016).

3.3.2 | Prunes in Allergy and Autoimmune Disease Modulation

Prunes contribute to immune regulation by modulating Th1/Th2 balance and reducing allergic responses. Karasawa et al. demonstrated that prune extract supplementation reduced sneezing frequency and specific IgE levels in a dust mite allergy mouse model. Prunes also increased the IFN-γ^+/IL-4^+ ratio in splenocytes, suggesting a shift toward Th1 dominance. Mechanistically, prunes regulate Stat6, Btk, and Stim1 pathways to balance Th1 and Th2 cells, reduce mast cell degranulation, and alleviate allergic reactions (Karasawa et al. 2012). In autoimmune diseases, Gupta et al. conducted computational simulations identifying four peptides (HLLP, LPLL, LPAGV, and NLPL) derived from prune seeds that inhibit IL-17A and IL-23 activity. This suggests a potential therapeutic effect on SLE by reducing proinflammatory cytokine activity (Gupta et al. 2024).

Prunes can mitigate joint damage and inflammation in arthritis models by targeting both inflammatory and bone resorption pathways. Mirza et al. found that a 20% prune diet over 4 weeks reduced arthritis onset and bone erosion in TNF-overexpressing transgenic mice. It also lowered the generation of TRAP-positive osteoclasts, preserved cartilage, and reduced synovitis. Neochlorogenic acid, a major polyphenol in prunes, was identified as a key bioactive compound. It inhibits NF-κB activation and NFATc1 expression while downregulating proinflammatory cytokines like IL-1β, MCP1, MIP1α, MMP1 & 3, and RANKL (Mirza et al. 2018).

3.3.3 | Prunes as Therapeutic Nanoparticle Carriers and Specialized Anti-Inflammatory Compounds

Prunes also serve as an innovative platform for delivering anti-inflammatory agents and specialized bioactives. Islam et al. explored the use of gum-stabilized gold and silver nanoparticles (Au/Ag-NPs) derived from prunes in a carrageenan-induced paw edema model. At doses of 40 and 80 mg/kg, the nanoparticles significantly alleviated inflammation (Islam et al. 2017). Meanwhile, Youssef et al. studied the lignan glycoside pinoresinol-4-*O*-β-D-glucopyranoside (PGu) isolated from prunes in a lithium/pilocarpine-induced epilepsy model in rats. PGu reduced COX-2 and iNOS expression and delayed the onset of seizures in a dose-dependent manner, improving survival rates and reducing seizure frequency (Youssef, Menze, et al. 2020).

3.4 | Glycolipid Metabolism Regulation Effects

Disorders related to glucose and lipid metabolism, including diabetes, obesity, nonalcoholic fatty liver disease (NAFLD), hypertension, and cardiovascular diseases, represent a significant global health burden. These conditions are strongly linked to unhealthy dietary patterns, insufficient physical activity, genetic predisposition, and environmental factors (Haddadi-Guemghar et al. 2017; G. Noratto et al. 2015; Walkowiak-Tomczak et al. 2018; Youssef, Ashour, et al. 2020). High-risk populations include individuals with a family history of metabolic disorders, elderly individuals, people with obesity, those consuming prolonged high-sugar and high-fat diets, sedentary individuals, and those exposed to occupational risks (Ioannou 2021). The impact of these diseases is profound, leading to reduced quality of life and increased risks of severe complications, such as cardiovascular diseases, kidney failure, and stroke, which can significantly raise mortality rates. Addressing these challenges requires effective interventions targeting both prevention and management.

Emerging evidence highlights the potential of prunes and their bioactive components in improving glucose and lipid metabolism. Studies have shown that prunes and prune extracts exert beneficial effects on hyperhomocysteinemia (Haddadi-Guemghar et al. 2017), obesity (G. Noratto et al. 2015), type 1 diabetes (Youssef, Ashour, et al. 2020), and hypercholesterolemia (Walkowiak-Tomczak et al. 2018; Table 2).

3.4.1 | Impact of Prunes on Hyperhomocysteinemia and Associated Health Risks

Hyperhomocysteinemia refers to a metabolic condition characterized by elevated levels of homocysteine (Hcy) in the blood. Hcy is a sulfur-containing amino acid produced during the metabolism of methionine. Under normal physiological conditions, Hcy is metabolized through several key pathways, including remethylation to methionine, transsulfuration to cysteine, and conversion to S-adenosylhomocysteine (SAH). Disruptions in these metabolic pathways can lead to an accumulation of Hcy, resulting in hyperhomocysteinemia (Li et al. 2018). This condition has been linked to a range of serious health issues, including cardiovascular diseases, stroke, thrombosis, diabetes, Alzheimer's disease, and cognitive decline (Kim et al. 2018). Hyperhomocysteinemia is considered an independent risk factor for these conditions, highlighting its clinical significance. In this context, Haddadi-Guemghar et al. explored the effects of prune extract on hyperhomocysteinemia in a mouse model. The researchers induced hyperhomocysteinemia by knocking out the *Cbs* gene and administered prune extract via intraperitoneal injection. The study found that prune extract significantly reduced Hcy levels by enhancing the activity of S-adenosylhomocysteine hydrolase (SAHH), a key enzyme responsible for converting Hcy to SAH. Importantly, the increase in SAHH activity was linked to a corresponding rise in the activity of NAD(P)H: quinone oxidoreductase 1 (NQO1), an enzyme involved in NAD^+ production. NAD^+ serves as a crucial cofactor for SAHH, suggesting a mechanistic

TABLE 2 | Effects of prune on glucose and lipid metabolism.

Problems	Prune materials	Model	Improvement	Mechanism	References
Hyperhomocysteinemia	Polyphenols	$Cbs^{+/-}$ mice	Plasma homocysteine level ↓	SAHH ↑ NQO1 ↑	Haddadi-Guemghar et al. (2017)
Obesity	Juice	Zucker-$Lepr^{fa}$/$Lepr^{+}$ rats	Less 16% weight gain Lower blood sugar, insulin and leptin levels HDL-CHL/T-CHL ↑ T-CHL ↓ non–HDL-CHL ↓ TG ↓ Prevented fat accumulation in the liver and heart	PPAR-γ ↑ ICAM-1 ↓ VCAM-1 ↓ NF-κB ↓	G. Noratto et al. (2015)
	Polyphenols	In vitro enzyme activity	Pancreatic lipase activity ↓ 15-LOX ↓	\	Rybak and Wojdylo (2023)
Hyperglycemia	Pinoresinol-4-*O*-β-D-glucopyranoside	STZ induced type 1 diabetic mice	Reduced 37.83% serum glucose levels Increased 25.37% insulin levels AST ↓ ALT ↓	PPARγ ↑ HPA ↓ HAG ↓	Youssef, Ashour, et al. (2020)
	Polyphenols	In vitro enzyme activity	α-Amylase ↓ α-Glucosidase ↓	\	Rybak and Wojdylo (2023)
	Purunusides	In vitro enzyme activity	α-Glucosidase ↓	\	Kosar et al. (2009)
	Prune	Randomized parallel arm trial, overweight healthy volunteers	TAC ↑ Lower postprandial insulin responses Lower LDL-c Lower LDL-c/HDL-c	\	Clayton et al. (2019)

(Continues)

TABLE 2 | (Continued)

Problems	Prune materials	Model	Improvement	Mechanism	References
Hypercholesterolemia	Prune	Clinical trials with 48 individuals with serum TC ≥ 200 mg/dL	TC LDL-c LDL-c/HDL-c	\	Walkowiak-Tomczak et al. (2018)
	Prune essence concentrate	Placebo-controlled, randomized study with 60 healthy mild hypercholesterolemic subjects	TC ↓ LDL-c ↓ *Bifidobacterium* spp. ↑ *Lactobacillus* spp. ↑ *Clostridium perfringens* ↓ *Escherichia coli* ↓	\	Chiu et al. (2017)
	Prune	Parallel-arm, randomized controlled trial with 48 healthy postmenopausal women	TC ↓ HDL-c ↑ TC/HDL-c ↓ IL-6, TNF-α ↓ TBARS ↓ SOD ↑	\	Hong et al. (2021)

pathway through which prunes may exert their beneficial effects in reducing Hcy levels (Haddadi-Guemghar et al. 2017).

3.4.2 | Prunes as a Dietary Intervention in Obesity Management

Obesity has become a global health crisis, with its prevalence increasing steadily over the past few decades. It is a complex metabolic disorder characterized by excessive fat accumulation, leading to an elevated risk of numerous chronic conditions. Obesity is typically caused by an imbalance between energy intake and energy expenditure. The mechanisms underlying obesity involve dysregulation of lipid metabolism, insulin resistance, and chronic low-grade inflammation, all of which contribute to the development of comorbidities (Backhed et al. 2007). Research into potential dietary interventions to mitigate obesity has gained attention, with certain functional foods, like prunes, showing promise in preventing or managing obesity and its associated metabolic disturbances (G. Noratto et al. 2015; Rybak and Wojdylo 2023). Noratto et al. evaluated the antiobesity effects of prune juice using Zucker-Lepr^{fa}/Lepr^{+} rats, a commonly used model for obesity studies. The results showed that prune juice helped maintain lower levels of blood glucose, insulin, and leptin, and significantly prevented weight gain, with a reduction of approximately 16% compared to the control group (G. Noratto et al. 2015). Additionally, prune juice was found to improve obesity-induced dyslipidemia by lowering total cholesterol (T-CHL), non–high-density lipoprotein cholesterol (non–HDL-CHL), and triglyceride (TG) levels in plasma. The authors suggested that the antiobesity effects of prune juice might be related to the activation of peroxisome proliferator-activated receptor gamma (PPAR-γ). They hypothesized that the polyphenols in prunes could act as PPAR-γ agonists, inhibiting the expression of cell adhesion molecules (ICAM-1 and VCAM-1), preventing NF-κB activation, and ultimately reducing biomarkers associated with obesity and inflammation (G. Noratto et al. 2015). Rybak et al. investigated the inhibitory effects of polyphenolic compounds in prunes on pancreatic lipase (Rybak and Wojdylo 2023). Pancreatic lipase is responsible for hydrolyzing the ester bonds at the 1- and 3-positions of TGs, progressively breaking them down into monoglycerides and fatty acids. These products form mixed micelles with bile salts, which facilitate the absorption of fats through the intestinal mucosa. The absorbed fatty acids and monoglycerides are then re-esterified into TGs within the enterocytes and transported into the bloodstream via chylomicrons. The study found that the polyphenols in prunes could inhibit pancreatic lipase activity, potentially reducing fat absorption and helping to mitigate obesity.

3.4.3 | Prunes in Hyperglycemia Control and Insulin Sensitivity Enhancement

Hyperglycemia, or elevated blood glucose levels, is a common metabolic disorder that occurs when the body is unable to effectively regulate blood sugar. It is often associated with insulin resistance or insufficient insulin production, and is a hallmark of conditions like diabetes mellitus. Chronic hyperglycemia can lead to a wide range of health complications, including cardiovascular diseases, kidney dysfunction, nerve damage, and an increased risk of stroke (Campos 2012). Management of hyperglycemia is essential for reducing the risk of these complications, and dietary interventions are increasingly recognized as an important strategy in the management and prevention of hyperglycemia (Davies et al. 2018). Youssef et al. investigated the role of PGu in suppressing hyperglycemia in type 1 diabetes. Their study, using streptozotocin (STZ)-induced diabetic mice, found that PGu significantly reduced serum glucose levels by 37.83%, while increasing insulin levels by 25.37% (Youssef, Ashour, et al. 2020). The mechanism of action suggested that PGu inhibited both α-glucosidase and α-amylase, enzymes responsible for the breakdown of carbohydrates into glucose. Additionally, PGu demonstrated high affinity for PPARγ, which may help improve insulin resistance by stimulating glucose oxidation and reducing free fatty acids. The compound also interacted with the active site of aldose reductase (AR), a key enzyme in diabetic complications, further supporting its potential therapeutic effects on diabetes and its complications. Rybak et al. found that polyphenols in prunes could inhibit α-amylase and α-glucosidase activities, which may contribute to the reduction of blood glucose levels (Rybak and Wojdylo 2023). Furthermore, Kosar et al. isolated three isoflavone glucosides, named Purunusides A–C, from prunes. These compounds exhibited significant inhibitory activity against α-glucosidase, potentially aiding in the regulation of blood glucose levels and improving both glucose and lipid metabolism (Kosar et al. 2009). In a randomized parallel-arm trial, Clayton et al. observed that, compared to refined carbohydrate snacks (low-fat muffins), prunes significantly reduced postprandial insulin responses after 8 weeks. This suggests that prunes play a role in regulating glucose metabolism in overweight adults (Clayton et al. 2019).

3.4.4 | Cholesterol-Lowering and Anti-Inflammatory Effects of Prunes

Hypercholesterolemia, characterized by elevated levels of cholesterol in the blood, particularly LDL-c, is a major risk factor for cardiovascular diseases, including atherosclerosis and coronary heart disease (Wadhera et al. 2016). This condition often results from unhealthy dietary habits, lack of physical activity, and genetic predisposition. Factors such as obesity, high intake of saturated fats, and genetic mutations that affect lipid metabolism can contribute to the development of hypercholesterolemia (Kwiterovich Jr. 2002). The condition is closely associated with increased inflammation, oxidative stress, and endothelial dysfunction, which significantly increase the risk of atherosclerosis and other cardiovascular complications (Lahera et al. 2007). Managing cholesterol levels through lifestyle modifications and pharmacological interventions is critical to reduce the incidence of cardiovascular diseases. Walkowiak-Tomczak et al. recruited 48 participants with moderate hypercholesterolemia and demonstrated that a daily intake of 100 g of prune juice for 6 weeks resulted in significant reductions in TC, LDL-c, and the LDL/HDL cholesterol ratio (Walkowiak-Tomczak et al. 2018). In a meta-analysis, Askarpour et al. found that prunes significantly improved TC levels and reduced LDL-c in individuals with unhealthy lipid profiles (Askarpour et al. 2023). Chiu et al. conducted a RCT involving 60 healthy individuals with mild hypercholesterolemia. They reported that consumption of PEC significantly lowered both TC and LDL-c levels, while also promoting favorable changes in the gut microbiota. Specifically, PEC increased populations of beneficial bacteria such as *Bifidobacterium* spp. and *Lactobacillus* spp., while decreasing levels of harmful bacteria like *Clostridium perfringens* and *Escherichia coli*. The authors suggested that prunes' polyphenolic compounds might lower blood lipid levels by modulating gut microbiota composition, inhibiting cholesterol absorption, and enhancing bile acid excretion (Chiu et al. 2017). Furthermore, Hong et al. conducted a 6-month controlled clinical trial and found that prune consumption significantly reduced TC and increased high-density lipoprotein cholesterol (HDL-c) in postmenopausal women, thereby improving the TC/HDL-c ratio. Additionally, prune intake led to a notable decrease in inflammatory markers IL-6 and TNF-α, while enhancing antioxidant activity as evidenced by increased superoxide dismutase (SOD) levels (Hong et al. 2021).

3.5 | Antioxidant Effects

Oxidative stress refers to an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses. This imbalance plays a critical role in the development and progression of various diseases while also being involved in normal physiological functions, such as cell signaling (Wang et al. 2022). Oxidative stress is linked to several chronic conditions, including cardiovascular diseases, diabetes, and neurodegenerative disorders (Wang et al. 2022). It can disrupt cell structure and function, leading to cellular dysfunction or even cell death, which in turn promotes disease progression (Zhang et al. 2016). The causes of oxidative stress are diverse, including unhealthy lifestyle factors (such as smoking and alcohol consumption), environmental pollution, chronic infections, medication use, and nutritional deficiencies (Wang et al. 2022).

The polysaccharides, polyphenols, lignans, and other bioactive components in prunes have shown significant potential in regulating oxidative stress (Figure 5). Popov et al. compared the inhibitory effects of various prune pectin polysaccharides on superoxide anion radicals and found that PD-1, a pectin polysaccharide isolated via DEAE-cellulose column chromatography, exhibited the highest antioxidant activity. The authors suggested that this activity is likely linked to the presence of GalA residues in the pectin polysaccharides (Popov et al. 2014). Navarro-Hoyos et al. obtained the polyphenolic components of prunes through pressurized liquid extraction (PLE) under acidic and neutral conditions, then assessed their antioxidant capacity using DPPH and ORAC methods. They discovered that polyphenolic extracts from the neutral PLE conditions showed stronger antioxidant activity (Navarro-Hoyos et al. 2021). In another study by Navarro, it was found that prune peel exhibited higher antioxidant activity than the flesh. Correlation analysis revealed that proanthocyanidins were most strongly associated with this antioxidant capacity (Navarro et al. 2018). Drogoudi et al. also observed differences in antioxidant capacity between prune varieties and tissues. Prune peels contained higher levels of total phenols and antioxidant activity than flesh tissues. However, the peel-to-flesh ratio varied significantly among varieties, with differences reaching up to 6.6 times (Drogoudi and Pantelidis 2022). Lignans, another class of antioxidant compounds, also contribute to free radical scavenging. Youssef et al. evaluated the iron ion reduction ability (FRAP) and ABTS radical scavenging activity of PGu finding that its antioxidant activity was equivalent to 418.47 and 1091.3 μmol/g of ascorbic acid, respectively (Youssef, Ashour, et al. 2020). Kayano et al. isolated and identified ten compounds from prunes, including a novel bis-pyrrole compound and seven phenolic compounds that were isolated for the first time from prunes. Using the ORAC method, they assessed the antioxidant activity of these compounds and found that 3-caffeoylquinic acid methyl ester, 4-caffeoylquinic acid methyl ester, and caffeic acid methyl ester exhibited the highest ORAC values (Kayano, Kikuzaki, Ikami, et al. 2004). Kimura et al. employed antioxidant-guided isolation techniques to extract oligomeric proanthocyanidins from prune extracts. They used three methods: DPPH radical scavenging, an enzymatic system (XOD-NBT) to measure SOD activity, and a nonenzymatic system (PMS–NADH–NBT) for the same purpose. They found that the oligomeric proanthocyanidins in prunes exhibited stronger antioxidant activity than the well-known antioxidant CGA (Kimura et al. 2008). Kayano et al. also analyzed the content of caffeoylquinic acid (CQA) isomers in prunes using high-performance liquid chromatography (HPLC) and found that prunes contained relatively high levels of 4-*O*-caffeoylquinic acid. Using the ORAC method, they determined that CQA isomers contributed 28.4% to the overall antioxidant activity of prunes, suggesting the presence of other unidentified antioxidant components (Kayano, Kikuzaki, Yamada, et al. 2004).

Cultivation factors also play a role in influencing the antioxidant capacity of prunes. Trendafilova et al. explored how different rootstocks affect the antioxidant capacity of prunes and found that prunes grafted onto the "Wavit" rootstock contained higher levels of neochlorogenic acid, peonidin-3-*O*-rutinoside, cyanidin-3-*O*-rutinoside, and sucrose. These prunes also demonstrated stronger antioxidant activity in assays such as DPPH, ABTS, and FRAP (Trendafilova et al. 2022). Rashidinejad et al. compared the antioxidant capacities of prunes at various stages of ripening using FRAP and ABTS methods. They observed that as the fruit matured, both antioxidant activity and total phenolic content (TPC) declined (Rashidinejad and Ahmmed 2024).

Processing methods also significantly affect the antioxidant capacity of prunes. Michalska et al. compared the effects of various drying techniques on the antioxidant capacity of prune by-products and found that freeze-drying (FD) samples exhibited the highest antioxidant activity in both ABTS and FRAP assays, compared to convective drying (CD), microwave vacuum drying (MVD), and a combined process of convective predrying followed by MVD (CD/MVD). The authors speculated that the differences in antioxidant activity were related to changes in polyphenolic compounds, such as flavonoids and anthocyanins, during the other drying processes (Michalska, Wojdylo, Majerska, et al. 2019). Silvan et al. also assessed the impact of different drying techniques on prune antioxidant capacity, with a focus on the effect of prune extracts on ROS levels in HT-29 cells, measured using the DCFH-DA probe. They found that spray-dried prunes had stronger ROS scavenging ability than both vacuum-dried and freeze-dried samples, reducing ROS production by nearly 37% compared to the oxidative control group (Silvan et al. 2020). Rippin et al. compared the antioxidant activity of prunes before and after treatment with tannin acyl hydrolase (tannase).

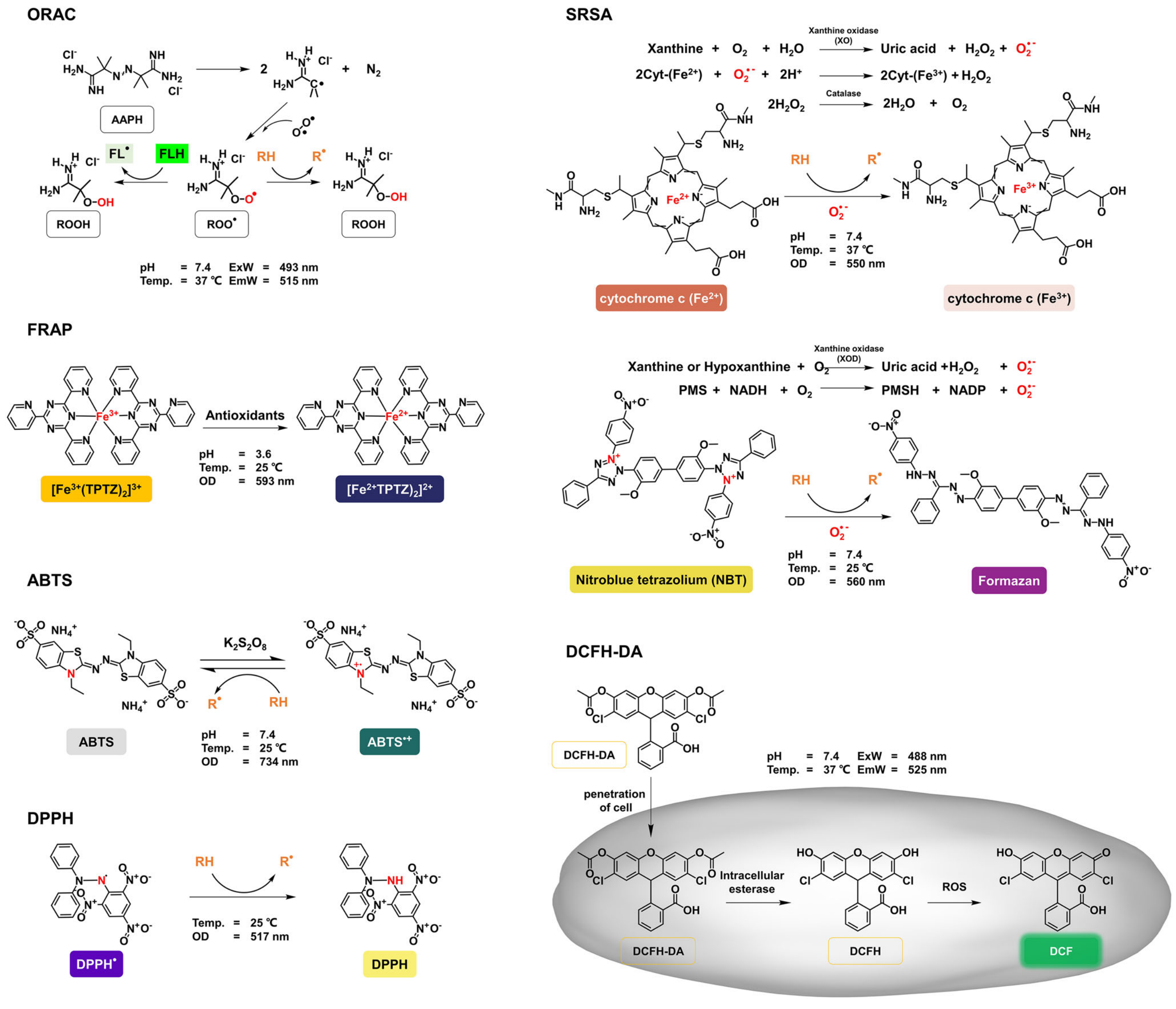

FIGURE 5 | Antioxidant effects of prunes.

They observed that tannase treatment enhanced the antioxidant activity of prune extracts, likely due to the hydrolysis of tannins into gallic acid and other antioxidant metabolites (Rippin et al. 2023).

Different extraction methods also influence the antioxidant capacity of prunes. Savic et al. assessed the antioxidant activity of fixed oil extracts from prune seeds using various solvents and found that the oil extracted with a chloroform:methanol (2:1 v/v) mixture exhibited the highest antioxidant activity (Savic et al. 2020). Najafabad et al. compared the antioxidant capacities of prune extracts obtained with methanol and ethanol as solvents. They found that the ethanol extract from fresh samples demonstrated the strongest ability to inhibit ROS production (Morabbi Najafabad and Jamei 2014).

4 | Outlook

Prunes (*Prunus domestica* L.) have long been recognized as a functional food with promising health benefits due to their rich bioactive components, including polyphenols, dietary fiber, lignans, and sorbitol. While significant progress has been made in understanding their biological effects, a more comprehensive exploration of their mechanisms and clinical applications is necessary. The following research directions are pivotal for maximizing the potential of prunes as a functional food and therapeutic agent.

4.1 | Identification of Active Compounds

Future research can further explore the bioactive compounds in prunes, particularly trace components that may have significant impacts on human health. Modern separation and analytical techniques, such as HPLC, mass spectrometry (MS), and nuclear magnetic resonance (NMR), can be used to more accurately identify and quantify these compounds. Additionally, researchers could investigate the active compounds in prune by-products to maximize resource utilization and develop new functional foods and supplements.

4.2 | Determining Effective Doses

A critical gap in current research is the lack of standardized dose–response data for prunes and their bioactive compounds. Studies on prune extracts often vary in dosage, making it difficult to assess their optimal levels for health benefits. Establishing precise dose–response relationships is essential to determine the effective and safe dosages of prunes in clinical and dietary contexts.

Further research is needed to assess the bioactivity of prunes at varying doses, taking into account factors such as the form of consumption (fresh, dried, or extract), as well as individual variability (e.g., age, gender, and health status). This will provide the scientific foundation necessary for the development of health guidelines and help ensure that prune-based interventions are both effective and safe for widespread use.

4.3 | Mechanism Research and Multiomics Integration

While the antioxidant, anti-inflammatory, and digestive health benefits of prunes are well established, the underlying molecular mechanisms remain insufficiently understood. Future research should aim to elucidate the specific molecular pathways through which prunes exert their effects.

Integrating multiomics technologies, including genomics, transcriptomics, and metabolomics, with cell models, animal studies, and clinical trials, could provide deeper insights into how prune components, such as polyphenols, sorbitol, and dietary fiber, influence key biological processes. Importantly, research should also focus on how these mechanisms are linked to disease prevention, particularly for chronic conditions such as cardiovascular diseases, diabetes, osteoporosis, and neurodegenerative disorders. Understanding the interaction between prune bioactives and disease-related pathways would demonstrate the practical health benefits of prunes and further validate their role in disease prevention and management. For example, how antioxidants in prunes reduce oxidative stress and inflammation could have implications for reducing the risk of cardiovascular diseases or improving bone health in osteoporosis.

4.4 | Clinical Validation and Personalized Nutrition

Although existing studies show significant health benefits of prunes in multiple areas, clinical evidence for their application remains limited. Future research should conduct more large-scale RCTs, particularly among high-risk populations such as the elderly, obese individuals, diabetic patients, and those with osteoporosis. Additionally, with the development of precision medicine, integrating individual genetic information and metabolic profiles will help identify the differential effects of prunes in different individuals, providing valuable references for personalized nutrition strategies.

Author Contributions

Luyang Han and Tiantian Fu were involved in the conception and design, or analysis and interpretation of the data; Luyang Han, Menglin Zhou, Jinhu Tian, Yaqun Liu, Feifei Gao, and Yue Wang drafted the paper; Manxi Wu, Han Yang, Jinping Cao, and Chongde Sun revised the manuscript critically for intellectual content; Chongde Sun and Yue Wang were involved in the final approval of the version to be published. All the authors agreed to be accountable for all aspects of the work.

Acknowledgments

This article was supported by the National Key Research and Development Program (2024YFD2100104), the Basic Public Welfare Research Program of Zhejiang Province (LBY24H040004), the National Natural Science Foundation of China (32101932), the Zhejiang Key R&D Development Project (2024C04030), the Fundamental Research Funds for the Zhejiang Provincial Universities (226-2024-00211).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

No data were used for the research described in the article.

References

Alarcon-Segovia, D., M. E. Alarcon-Riquelme, M. H. Cardiel, et al. 2005. "Familial Aggregation of Systemic Lupus Erythematosus, Rheumatoid Arthritis, and Other Autoimmune Diseases in 1,177 Lupus Patients From the GLADEL Cohort." *Arthritis and Rheumatism* 52, no. 4: 1138–1147. http://doi.org/10.1002/art.20999.

Al-Dashti, Y. A., R. R. Holt, J. G. Carson, C. L. Keen, and R. M. Hackman. 2019. "Effects of Short-Term Dried Plum (Prune) Intake on Markers of Bone Resorption and Vascular Function in Healthy Postmenopausal Women: A Randomized Crossover Trial." *Journal of Medicinal Food* 22, no. 10: 982–992. http://doi.org/10.1089/jmf.2018.0209.

Askarpour, M., H. Ghalandari, L. Setayesh, and E. Ghaedi. 2023. "Plum Supplementation and Lipid Profile: A Systematic Review and Meta-Analysis of Randomised Controlled Trials." *Journal of Nutritional Science* 12: e6. http://doi.org/10.1017/jns.2022.101.

Attaluri, A., R. Donahoe, J. Valestin, K. Brown, and S. S. Rao. 2011. "Randomised Clinical Trial: Dried Plums (Prunes) Vs. Psyllium for Constipation." *Alimentary Pharmacology & Therapeutics* 33, no. 7: 822–828. http://doi.org/10.1111/j.1365-2036.2011.04594.x.

Backhed, F., J. K. Manchester, C. F. Semenkovich, and J. I. Gordon. 2007. "Mechanisms Underlying the Resistance to Diet-Induced Obesity in Germ-Free Mice." *PNAS* 104, no. 3: 979–984. http://doi.org/10.1073/pnas.0605374104.

Banu, J. 2013. "Causes, Consequences, and Treatment of Osteoporosis in Men." *Drug Design, Development and Therapy* 7: 849–860. http://doi.org/10.2147/DDDT.S46101.

Basso, P., M. Fonseca, G. Bonfá, et al. 2014. "Association Among Genetic Predisposition, Gut Microbiota, and Host Immune Response in the Etiopathogenesis of Inflammatory Bowel Disease." *Brazilian Journal of Medical and Biological Research* 47, no. 9: 727–737. http://doi.org/10.1590/1414-431x20143932.

Bei, M. F., A. I. Apahidean, R. Budău, et al. 2024. "An Overview of the Phytochemical Composition of Different Organs of *Prunus spinosa* L., Their Health Benefits and Application in Food Industry." *Horticulturae* 10, no. 1: 29. https://doi.org/10.3390/horticulturae10010029.

Campos, C. 2012. "Chronic Hyperglycemia and Glucose Toxicity: Pathology and Clinical Sequelae." *Postgraduate Medicine* 124, no. 6: 90–97. http://doi.org/10.3810/pgm.2012.11.2615.

Cantu-Jungles, T. M., D. Maria-Ferreira, L. M. da Silva, et al. 2014. "Polysaccharides From Prunes: Gastroprotective Activity and Structural Elucidation of Bioactive Pectins." *Food Chemistry* 146: 492–499. http://doi.org/10.1016/j.foodchem.2013.09.093.

Cheng, C., A. O. Chan, W. M. Hui, and S. K. Lam. 2003. "Coping Strategies, Illness Perception, Anxiety and Depression of Patients With Idiopathic Constipation: A Population-Based Study." *Alimentary Pharmacology & Therapeutics* 18, no. 3: 319–326. http://doi.org/10.1046/j.1365-2036.2003.01663.x.

Chey, S. W., W. D. Chey, K. Jackson, and S. Eswaran. 2021. "Exploratory Comparative Effectiveness Trial of Green Kiwifruit, Psyllium, or Prunes in US Patients With Chronic Constipation." *American Journal of Gastroenterology* 116, no. 6: 1304–1312. http://doi.org/10.14309/ajg.0000000000001149.

Chinen, J., and W. T. Shearer. 2010. "Secondary Immunodeficiencies, Including HIV Infection." *Journal of Allergy and Clinical Immunology* 125: no. 2 suppl. 2: S195–203. http://doi.org/10.1016/j.jaci.2009.08.040.

Chiu, H. F., Y. C. Huang, Y. Y. Lu, et al. 2017. "Regulatory/Modulatory Effect of Prune Essence Concentrate on Intestinal Function and Blood Lipids." *Pharmaceutical Biology* 55, no. 1: 974–979. http://doi.org/10.1080/13880209.2017.1285323.

Cinquanta, L., M. Di Matteo, and M. Esti. 2002. "Physical Pre-Treatment of Plums (*Prunus domestica*). Part 2. Effect on the Quality Characteristics of Different Prune Cultivars." *Food Chemistry* 79, no. 2: 233–238. http://doi.org/10.1016/s0308-8146(02)00138-3.

Clayton, Z. S., E. Fusco, L. Schreiber, et al. 2019. "Snack Selection Influences Glucose Metabolism, Antioxidant Capacity and Cholesterol in Healthy Overweight Adults: A Randomized Parallel Arm Trial." *Nutrition Research* 65: 89–98. http://doi.org/10.1016/j.nutres.2019.03.002.

Damani, J. J., M. J. De Souza, H. L. VanEvery, N. C. A. Strock, and C. J. Rogers. 2022. "The Role of Prunes in Modulating Inflammatory Pathways to Improve Bone Health in Postmenopausal Women." *Advances in nutrition* 13, no. 5: 1476–1492. http://doi.org/10.1093/advances/nmab162.

Davies, M. J., D. A. D'Alessio, J. Fradkin, et al. 2018. "Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)." *Diabetes Care* 41, no. 12: 2669–2701. http://doi.org/10.2337/dci18-0033.

Delgado Cuenca, P., L. Almaiman, S. Schenk, M. Kern, and S. Hooshmand. 2017. "Dried Plum Ingestion Increases the Osteoblastogenic Capacity of Human Serum." *Journal of Medicinal Food* 20, no. 7: 653–658. http://doi.org/10.1089/jmf.2016.0158.

de Souza, M. J., N. C. Strock, N. I. Williams, et al. 2022. "Prunes Preserve Hip Bone Mineral Density in a 12-Month Randomized Controlled Trial in Postmenopausal Women: The Prune Study." *American Journal of Clinical Nutrition* 116, no. 4: 897–910. https://doi.org/10.1093/ajcn/nqac189.

Deyhim, F., B. J. Stoecker, G. H. Brusewitz, L. Devareddy, and B. H. Arjmandi. 2005. "Dried Plum Reverses Bone Loss in an Osteopenic Rat Model of Osteoporosis." *Menopause* 12, no. 6: 755–762. http://doi.org/10.1097/01.gme.0000185486.55758.5b.

Drogoudi, P., and G. Pantelidis. 2022. "Phenotypic Variation and Peel Contribution to Fruit Antioxidant Contents in European and Japanese Plums." *Plants (Basel)* 11, no. 10: 1338. http://doi.org/10.3390/plants11101338.

Dugalic, K., R. Sudar, M. Viljevac, M. Josipovic, and T. Cupic. 2014. "Sorbitol and Sugar Composition in Plum Fruits Influenced by Climatic Conditions." *Journal of Agricultural Science and Technology-Iran* 16, no. 5: 1145–1155.

Fatimi, A., M. c. Ralet, M. J. Crepeau, S. Rashidi, and J. F. Thibault. 2007. "Dietary Fibre Content and Cell Wall Polysaccharides in Prunes." *Sciences Des Aliments* 27, no. 6: 423–429. http://doi.org/10.3166/sda.27.423-430.

George, K. S., J. Munoz, L. T. Ormsbee, et al. 2022. "The Short-Term Effect of Prunes in Improving Bone in Men." *Nutrients* 14, no. 2: 276. http://doi.org/10.3390/nu14020276.

Gill, S. K., E. Lever, P. W. Emery, and K. Whelan. 2019. "Nutrient, Fibre, Sorbitol and Chlorogenic Acid Content of prunes (*Prunus domestica*): An Updated Analysis and Comparison of Different Countries of Origin and Database Values." *International Journal of Food Science and Nutrition* 70, no. 8: 924–931. http://doi.org/10.1080/09637486.2019.1600664.

Graef, J. L., E. Rendina-Ruedy, E. K. Crockett, et al. 2018. "Select Polyphenolic Fractions From Dried Plum Enhance Osteoblast Activity Through BMP-2 Signaling." *Journal of Nutritional Biochemistry* 55: 59–67. http://doi.org/10.1016/j.jnutbio.2017.09.014.

Gupta, A., T. Jamal, P. Rajbhar, A. S. Gaur, S. S. Chauhan, and R. Parthasarathi. 2024. "Cytokines Inhibitory Mechanism of *Prunus domestica* L. (Plum) Peptides as Potential Immunomodulators Against Systemic Lupus Erythematosus: An In-Silico Screening." *In Silico Pharmacology* 12, no. 1: 12. http://doi.org/10.1007/s40203-023-00188-8.

Haddadi-Guemghar, H., A. Tlili, J. Dairou, J. L. Paul, K. Madani, and N. Janel. 2017. "Effect of Lyophilized Prune Extract on Hyperhomocysteinemia in Mice." *Food and Chemical Toxicology* 103: 183–187. http://doi.org/10.1016/j.fct.2017.03.018.

Higgins, P. D., and J. F. Johanson. 2004. "Epidemiology of Constipation in North America: A Systematic Review." *American Journal of Gastroenterology* 99, no. 4: 750–759. https://doi.org/10.1111/j.1572-0241.2004.04114.x.

Hong, M. Y., M. Kern, M. Nakamichi-Lee, N. Abbaspour, A. Ahouraei Far, and S. Hooshmand. 2021. "Dried Plum Consumption Improves Total Cholesterol and Antioxidant Capacity and Reduces Inflammation in Healthy Postmenopausal Women." *Journal of Medicinal Food* 24, no. 11: 1161–1168. http://doi.org/10.1089/jmf.2020.0142.

Hooshmand, S., S. C. Chai, R. L. Saadat, M. E. Payton, K. Brummel-Smith, and B. H. Arjmandi. 2011. "Comparative Effects of Dried Plum and Dried Apple on Bone in Postmenopausal Women." *British Journal of Nutrition* 106, no. 6: 923–930. http://doi.org/10.1017/S000711451100119X.

Hooshmand, S., D. Gaffen, A. Eisner, J. Fajardo, M. Payton, and M. Kern. 2022. "Effects of 12 Months Consumption of 100 G Dried Plum (Prunes) on Bone Biomarkers, Density, and Strength in Men." *Journal of Medicinal Food* 25, no. 1: 40–47. http://doi.org/10.1089/jmf.2021.0080.

Hooshmand, S., M. Kern, D. Metti, et al. 2016. "The Effect of Two Doses of Dried Plum on Bone Density and Bone Biomarkers in Osteopenic Postmenopausal Women: A Randomized, Controlled Trial." *Osteoporosis International* 27, no. 7: 2271–2279. http://doi.org/10.1007/s00198-016-3524-8.

Hooshmand, S., A. Kumar, J. Y. Zhang, S. A. Johnson, S. C. Chai, and B. H. Arjmandi. 2015. "Evidence for Anti-Inflammatory and Antioxidative Properties of Dried Plum Polyphenols in Macrophage RAW 264.7 Cells." *Food & Function* 6, no. 5: 1719–1725. http://doi.org/10.1039/c5fo00173k.

Hull, C., R. S. Greco, and D. L. Brooks. 1980. "Alleviation of Constipation in the Elderly by Dietary Fiber Supplementation." *Journal of the American Geriatrics Society* 28, no. 9: 410–414. http://doi.org/10.1111/j.1532-5415.1980.tb01108.x.

Ioannou, G. N. 2021. "Epidemiology and Risk-Stratification of NAFLD-Associated HCC." *Journal of Hepatology* 75, no. 6: 1476–1484. http://doi.org/10.1016/j.jhep.2021.08.012.

Islam, N. U., R. Amin, M. Shahid, M. Amin, S. Zaib, and J. Iqbal. 2017. "A Multi-Target Therapeutic Potential of *Prunus domestica* Gum Stabilized Nanoparticles Exhibited Prospective Anticancer, Antibacterial, Urease-Inhibition, Anti-Inflammatory and Analgesic Properties." *BMC Complementary and Alternative Medicine [Electronic Resource]* 17, no. 1: 276. http://doi.org/10.1186/s12906-017-1791-3.

Kakkar, S., and S. Bais. 2014. "A Review on Protocatechuic Acid and Its Pharmacological Potential." *ISRN Pharmacology* 2014: 1–9. https://doi.org/10.1155/2014/952943.

Karasawa, K., R. Miyashita, and H. Otani. 2012. "Anti-Allergic Properties of a Fruit Extract of Prune (*Prunus domestica* L.) in Mite-Sensitized BALB/c Mice." *Food Science and Technology Research* 18, no. 5: 755–760. http://doi.org/10.3136/fstr.18.755.

Kaulmann, A., S. Legay, Y. J. Schneider, L. Hoffmann, and T. Bohn. 2016. "Inflammation Related Responses of Intestinal Cells to Plum and Cabbage Digesta With Differential Carotenoid and Polyphenol Profiles Following Simulated Gastrointestinal Digestion." *Molecular Nutrition & Food Research* 60, no. 5: 992–1005. http://doi.org/10.1002/mnfr.201500947.

Kayano, S., H. Kikuzaki, T. Ikami, T. Suzuki, T. Mitani, and N. Nakatani. 2004. "A New Bipyrrole and Some Phenolic Constituents in Prunes (*Prunus domestica* L.) and Their Oxygen Radical Absorbance Capacity (ORAC)." *Bioscience, Biotechnology, and Biochemistry* 68, no. 4: 942–944. http://doi.org/10.1271/bbb.68.942.

Kayano, S., H. Kikuzaki, N. F. Yamada, et al. 2004. "Antioxidant Properties of Prunes (*Prunus domestica* L.) and Their Constituents." *Biofactors* 21, no. 1–4: 309–313. http://doi.org/10.1002/biof.552210160.

Kim, J., H. Kim, H. Roh, and Y. Kwon. 2018. "Causes of Hyperhomocysteinemia and Its Pathological Significance." *Archives of Pharmacal Research* 41, no. 4: 372–383. http://doi.org/10.1007/s12272-018-1016-4.

Kimura, Y., H. Ito, M. Kawaji, T. Ikami, and T. Hatano. 2008. "Characterization and Antioxidative Properties of Oligomeric Proanthocyanidin From Prunes, Dried Fruit of *Prunus domestica* L." *Bioscience, Biotechnology, and Biochemistry* 72, no. 6: 1615–1618. http://doi.org/10.1271/bbb.70823.

Konrade, D., S. Gaidukovs, F. Vilaplana, and P. Sivan. 2023. "Pectin From Fruit- and Berry-Juice Production By-Products: Determination of Physicochemical, Antioxidant and Rheological Properties." *Foods* 12, no. 8: 1615. http://doi.org/10.3390/foods12081615.

Kosar, S., I. Fatima, A. Mahmood, et al. 2009. "Purunusides A-C, Alpha-Glucosidase Inhibitory Homoisoflavone Glucosides From *Prunus domestica*." *Archives of Pharmacal Research* 32, no. 12: 1705–1710. http://doi.org/10.1007/s12272-009-2207-9.

Kosmala, M., J. Milala, K. Kołodziejczyk, J. Markowski, M. Zbrzeźniak, and C. M. G. C. Renard. 2013. "Dietary Fiber and Cell Wall Polysaccharides From Plum (*Prunus domestica* L.) Fruit, Juice and Pomace: Comparison of Composition and Functional Properties for Three Plum Varieties." *Food Research International* 54, no. 2: 1787–1794. http://doi.org/10.1016/j.foodres.2013.10.022.

Koyama, T., N. Nagata, K. Nishiura, N. Miura, T. Kawai, and H. Yamamoto. 2022. "Prune Juice Containing Sorbitol, Pectin, and Polyphenol Ameliorates Subjective Complaints and Hard Feces While Normalizing Stool in Chronic Constipation: A Randomized Placebo-Controlled Trial." *American Journal of Gastroenterology* 117, no. 10: 1714–1717. http://doi.org/10.14309/ajg.0000000000001931.

Kwiterovich Jr, P. O. 2002. "Clinical Relevance of the Biochemical, Metabolic, and Genetic Factors That Influence Low-Density Lipoprotein Heterogeneity." *American Journal of Cardiology* 90, no. 8: 30–47. http://doi.org/10.1016/S0002-9149(02)02749-2.

Lahera, V., M. Goicoechea, S. G. de Vinuesa, et al. 2007. "Endothelial Dysfunction, Oxidative Stress and Inflammation in Atherosclerosis: Beneficial Effects of Statins." *Current Medicinal Chemistry* 14, no. 2: 243–248. http://doi.org/10.2174/092986707779313381.

Leotoing, L., F. Wauquier, M. J. Davicco, et al. 2016. "The Phenolic Acids of Agen Prunes (Dried Plums) or Agen Prune Juice Concentrates Do Not Account for the Protective Action on Bone in a Rat Model of Postmenopausal Osteoporosis." *Nutrition Research* 36, no. 2: 161–173. http://doi.org/10.1016/j.nutres.2015.10.002.

Lever, E., S. M. Scott, P. Louis, P. W. Emery, and K. Whelan. 2019. "The Effect of Prunes on Stool Output, Gut Transit Time and Gastrointestinal Microbiota: A Randomised Controlled Trial." *Clinical Nutrition* 38, no. 1: 165–173. http://doi.org/10.1016/j.clnu.2018.01.003.

Li, T., B. Yu, Z. Liu, et al. 2018. "Homocysteine Directly Interacts and Activates the Angiotensin II Type I Receptor to Aggravate Vascular Injury." *Nature Communications* 9, no. 1: 11. http://doi.org/10.1038/s41467-017-02401-7.

Limketkai, B. N., G. Godoy-Brewer, A. M. Parian, et al. 2023. "Dietary Interventions for the Treatment of Inflammatory Bowel Diseases: An Updated Systematic Review and Meta-Analysis." *Clinical Gastroenterology and Hepatology* 21, no. 10: 2508–2525e2510. http://doi.org/10.1016/j.cgh.2022.11.026.

Lin, Y., Y. Lin, H. Lin, et al. 2018. "Effects of Paper Containing 1-MCP Postharvest Treatment on the Disassembly of Cell Wall Polysaccharides and Softening in Younai Plum Fruit During Storage." *Food Chemistry* 264: 1–8. http://doi.org/10.1016/j.foodchem.2018.05.031.

Manach, C., A. Scalbert, C. Morand, C. Rémésy, and L. Jiménez. 2004. "Polyphenols: Food Sources and Bioavailability." *American Journal of Clinical Nutrition* 79, no. 5: 727–747. https://doi.org/10.1093/ajcn/79.5.727.

Michalska, A., J. Honke, G. Lysiak, and W. Andlauer. 2016. "Effect of Drying Parameters on the Formation of Early and Intermediate Stage Products of the Maillard Reaction in Different Plum (*Prunus domestica* L.) Cultivars." *LWT - Food Science and Technology* 65: 932–938. http://doi.org/10.1016/j.lwt.2015.09.015.

Michalska, A., A. Wojdylo, K. Lech, G. P. Lysiak, and A. Figiel. 2016. "Physicochemical Properties of Whole Fruit Plum Powders Obtained Using Different Drying Technologies." *Food Chemistry* 207: 223–232. http://doi.org/10.1016/j.foodchem.2016.03.075.

Michalska, A., A. Wojdylo, J. Majerska, K. Lech, and J. Brzezowska. 2019. "Qualitative and Quantitative Evaluation of Heat-Induced Changes in Polyphenols and Antioxidant Capacity in *Prunus domestica* L. By-Products." *Molecules (Basel, Switzerland)* 24, no. 16: 3008. http://doi.org/10.3390/molecules24163008.

Miletić, N., O. Mitrović, B. Popović, V. Nedović, B. Zlatković, and M. Kandić. 2013. "Polyphenolic Content and Antioxidant Capacity in Fruits of Plum (*Prunus domestica* L.) Cultivars "Valjevka" and "Mildora" as Influenced by Air Drying." *Journal of Food Quality* 36, no. 4: 229–237. http://doi.org/10.1111/jfq.12035.

Mirza, F., J. Lorenzo, H. Drissi, F. Y. Lee, and D. Y. Soung. 2018. "Dried Plum Alleviates Symptoms of Inflammatory Arthritis in TNF Transgenic Mice." *Journal of Nutritional Biochemistry* 52: 54–61. http://doi.org/10.1016/j.jnutbio.2017.10.002.

Mishra, S., and S. Vyas. 2021. "Therapeutic and Pharmacological Potential of Turmeric: An Overview." *International Journal of Pharmacognosy and Clinical Research* 12, no. 6: 3034–3041. https://doi.org/10.13040/IJPSR.0975-8232.12(6).3034-41.

Monsefi, M., F. Parvin, and M. Farzaneh. 2013. "Effects of Plum Extract on Skeletal System of Fetal and Newborn Mice." *Medical Principles and Practice* 22, no. 4: 351–356. http://doi.org/10.1159/000346625.

Morabbi Najafabad, A., and R. Jamei. 2014. "Free Radical Scavenging Capacity and Antioxidant Activity of Methanolic and Ethanolic Extracts of Plum (*Prunus domestica* L.) in Both Fresh and Dried Samples." *Avicenna Journal of Phytomedicine* 4, no. 5: 343–353. http://doi.org/10.22038/ajp.2014.2827.

Navarro, M., I. Moreira, E. Arnaez, et al. 2018. "Polyphenolic Characterization and Antioxidant Activity of *Malus domestica* and *Prunus domestica* Cultivars From Costa Rica." *Foods* 7, no. 2: 15. http://doi.org/10.3390/foods7020015.

Navarro-Hoyos, M., E. Arnáez-Serrano, S. Quesada-Mora, et al. 2021. "Polyphenolic QTOF-ESI MS Characterization and the Antioxidant and Cytotoxic Activities of *Prunus domestica* Commercial Cultivars From Costa Rica." *Molecules (Basel, Switzerland)* 26, no. 21: 6493. http://doi.org/10.3390/molecules26216493.

Nishida, M., K. Murata, Y. Kanamaru, and T. Yabe. 2014. "Pectin of *Prunus domestica* L. Alters Sulfated Structure of Cell-Surface Heparan Sulfate in Differentiated Caco-2 Cells Through Stimulation of Heparan Sulfate 6-*O*-Endosulfatase-2." *Bioscience, Biotechnology, and Biochemistry* 78, no. 4: 635–643. http://doi.org/10.1080/09168451.2014.891937.

Nishida, M., K. Murata, K. Oshima, et al. 2015. "Pectin From *Prunus domestica* L. Induces Proliferation of IEC-6 Cells Through the Alteration of Cell-Surface Heparan Sulfate on Differentiated Caco-2 Cells in Co-Culture." *Glycoconjugate Journal* 32, no. 3–4: 153–159. http://doi.org/10.1007/s10719-015-9588-4.

Niu, X. X., L. Z. Deng, H. Wang, et al. 2024. "Transformation of Cell Wall Pectin Profile During Postharvest Ripening Process Alters Drying Behavior and Regulates the Sugar Content of Dried Plums." *Food Chemistry* 458: 140093. http://doi.org/10.1016/j.foodchem.2024.140093.

Noratto, G., H. S. Martino, S. Simbo, D. Byrne, and S. U. Mertens-Talcott. 2015. "Consumption of Polyphenol-Rich Peach and Plum Juice Prevents Risk Factors for Obesity-Related Metabolic Disorders and Cardiovascular Disease in Zucker Rats." *Journal of Nutritional Biochemistry* 26, no. 6: 633–641. http://doi.org/10.1016/j.jnutbio.2014.12.014.

Noratto, G. D., J. F. Garcia-Mazcorro, M. Markel, et al. 2014. "Carbohydrate-Free Peach (*Prunus persica*) and Plum (*Prunus domestica*) Juice Affects Fecal Microbial Ecology in an Obese Animal Model." *PLoS ONE* 9, no. 7: e101723. http://doi.org/10.1371/journal.pone.0101723.

Nunes, C., L. Silva, A. P. Fernandes, R. P. F. Guine, M. R. M. Domingues, and M. A. Coimbra. 2012. "Occurrence of Cellobiose Residues Directly Linked to Galacturonic Acid in Pectic Polysaccharides." *Carbohydrate Polymers* 87, no. 1: 620–626. http://doi.org/10.1016/j.carbpol.2011.08.027.

Okawa, T., M. Nagai, and K. Hase. 2020. "Dietary Intervention Impacts Immune Cell Functions and Dynamics by Inducing Metabolic Rewiring." *Frontiers in Immunology* 11: 623989. http://doi.org/10.3389/fimmu.2020.623989.

Park, Y. S., H. W. Kim, J. H. Hwang, et al. 2023. "Plum-Derived Exosome-Like Nanovesicles Induce Differentiation of Osteoblasts and Reduction of Osteoclast Activation." *Nutrients* 15, no. 9: 2107. http://doi.org/10.3390/nu15092107.

Popov, S. V., R. G. Ovodova, V. V. Golovchenko, et al. 2014. "Pectic Polysaccharides of the Fresh Plum *Prunus domestica* L. Isolated With a Simulated Gastric Fluid and Their Anti-Inflammatory and Antioxidant Activities." *Food Chemistry* 143: 106–113. http://doi.org/10.1016/j.foodchem.2013.07.049.

Rashidinejad, A., and M. K. Ahmmed. 2024. "The Influence of Ripening on the Nutrient Composition and Antioxidant Properties of New Zealand Damson Plums." *Food Science & Nutrition* 12, no. 6: 4311–4320. http://doi.org/10.1002/fsn3.4097.

Renard, C. M. G. C., and C. Ginies. 2009. "Comparison of the Cell Wall Composition for Flesh and Skin From Five Different Plums." *Food Chemistry* 114, no. 3: 1042–1049. http://doi.org/10.1016/j.foodchem.2008.10.073.

Rippin, A. K. Sharma, and V. Beniwal. 2023. "Reconnoitring the Antioxidant and Antibacterial Potential of Different Fruits After Tannin Acyl Hydrolase Mediated Biotransformation." *Biotechnology and Applied Biochemistry* 70, no. 4: 1439–1449. http://doi.org/10.1002/bab.2461.

Rybak, M., and A. Wojdylo. 2023. "Inhibition of Alpha-Amylase, Alpha-Glucosidase, Pancreatic Lipase, 15-Lipooxygenase and Acetylcholinesterase Modulated by Polyphenolic Compounds, Organic Acids, and Carbohydrates of *Prunus domestica* Fruit." *Antioxidants (Basel)* 12, no. 7: 1380. http://doi.org/10.3390/antiox12071380.

Sahamishirazi, S., J. Moehring, W. Claupein, and S. Graeff-Hoenninger. 2017. "Quality Assessment of 178 Cultivars of Plum Regarding Phenolic, Anthocyanin and Sugar Content." *Food Chemistry* 214: 694–701. http://doi.org/10.1016/j.foodchem.2016.07.070.

Saini, R. K., and Y.-S. Keum. 2018. "Omega-3 and Omega-6 Polyunsaturated Fatty Acids: Dietary Sources, Metabolism, and Significance—A Review." *Life Sciences* 203: 255–267. https://doi.org/10.1016/j.lfs.2018.04.049.

Sairanen, U., L. Piirainen, R. Nevala, and R. Korpela. 2007. "Yoghurt Containing Galacto-Oligosaccharides, Prunes and Linseed Reduces the Severity of Mild Constipation in Elderly Subjects." *European Journal of Clinical Nutrition* 61, no. 12: 1423–1428. http://doi.org/10.1038/sj.ejcn.1602670.

Santana-Gálvez, J., L. Cisneros-Zevallos, and D. Jacobo-Velázquez. 2017. "Chlorogenic Acid: Recent Advances on Its Dual Role as a Food Additive and a Nutraceutical Against Metabolic Syndrome." *Molecules (Basel, Switzerland)* 22, no. 3: 358. https://doi.org/10.3390/molecules22030358.

Savic, I., I. Savic Gajic, and D. Gajic. 2020. "Physico-Chemical Properties and Oxidative Stability of Fixed Oil From Plum Seeds (*Prunus domestica* Linn.)." *Biomolecules* 10, no. 2: 294. http://doi.org/10.3390/biom10020294.

Schreurs, A. S., Y. Shirazi-Fard, M. Shahnazari, et al. 2016. "Dried Plum Diet Protects From Bone Loss Caused by Ionizing Radiation." *Scientific Reports* 6: 21343. http://doi.org/10.1038/srep21343.

Shahnazari, M., R. T. Turner, U. T. Iwaniec, et al. 2016. "Dietary Dried Plum Increases Bone Mass, Suppresses Proinflammatory Cytokines and Promotes Attainment of Peak Bone Mass in Male Mice." *Journal of Nutritional Biochemistry* 34: 73–82. http://doi.org/10.1016/j.jnutbio.2016.04.007.

Shukla, R. K., and Kishan. 2021. "A Review on European Plum (*Prunus domestica*) for Its Pharmacological Activities and Phytochemicals." *Research Journal of Pharmacy and Technology* 14, no. 2: 1155–1162. https://doi.org/10.5958/0974-360x.2021.00207.9.

Silvan, J. M., A. Michalska-Ciechanowska, and A. J. Martinez-Rodriguez. 2020. "Modulation of Antibacterial, Antioxidant, and Anti-Inflammatory Properties by Drying of *Prunus domestica* L. Plum Juice Extracts." *Microorganisms* 8, no. 1: 119. http://doi.org/10.3390/microorganisms8010119.

Simpson, A. M. R., M. J. De Souza, J. Damani, et al. 2022. "Prune Supplementation for 12 Months Alters the Gut Microbiome in Postmenopausal Women." *Food & Function* 13, no. 23: 12316–12329. http://doi.org/10.1039/d2fo02273g.

Smith, B. J., B. Hatter, K. Washburn, et al. 2022. "Dried Plum's Polyphenolic Compounds and Carbohydrates Contribute to Its Osteoprotective Effects and Exhibit Prebiotic Activity in Estrogen Deficient C57BL/6 Mice." *Nutrients* 14, no. 9: 1685. http://doi.org/10.3390/nu14091685.

Stacewicz-Sapuntzakis, M. 2013. "Dried Plums and Their Products: Composition and Health Effects–An Updated Review." *Critical Reviews in Food Science and Nutrition* 53, no. 12: 1277–1302. http://doi.org/10.1080/10408398.2011.563880.

Stacewicz-Sapuntzakis, M., P. E. Bowen, E. A. Hussain, B. I. Damayanti-Wood, and N. R. Farnsworth. 2001. "Chemical Composition and Potential Health Effects of Prunes: A Functional Food?" *Critical Reviews in Food Science and Nutrition* 41, no. 4: 251–286. http://doi.org/10.1080/20014091091814.

Steczina, S., C. G. T. Tahimic, M. Pendleton, et al. 2020. "Dietary Countermeasure Mitigates Simulated Spaceflight-Induced Osteopenia in Mice." *Scientific Reports* 10, no. 1: 6484. http://doi.org/10.1038/s41598-020-63404-x.

Tajik, N., M. Tajik, I. Mack, and P. Enck. 2017. "The Potential Effects of Chlorogenic Acid, the Main Phenolic Components in Coffee, on Health: A Comprehensive Review of the Literature." *European Journal of Nutrition* 56, no. 7: 2215–2244. https://doi.org/10.1007/s00394-017-1379-1.

Tomic, J., F. Stampar, I. Glisic, and J. Jakopic. 2019. "Phytochemical Assessment of Plum (*Prunus domestica* L.) Cultivars Selected in Serbia." *Food Chemistry* 299: 125113. http://doi.org/10.1016/j.foodchem.2019.125113.

Trendafilova, A., V. Ivanova, B. Trusheva, M. Kamenova-Nacheva, S. Tabakov, and S. Simova. 2022. "Chemical Composition and Antioxidant Capacity of the Fruits of European Plum Cultivar "*Cacanska lepotica*" Influenced by Different Rootstocks." *Foods* 11, no. 18: 2844. http://doi.org/10.3390/foods11182844.

Udenigwe, C. C., and R. E. Aluko. 2011. "Food Protein-Derived Bioactive Peptides: Production, Processing, and Potential Health Benefits." *Journal of Food Science* 77, no. 1: R11–24. https://doi.org/10.1111/j.1750-3841.2011.02455.x.

Usenik, V. 2021. "The Influence of the Production System on the Composition of Phytochemicals in *Prunus domestica* L. fruit." *Journal of Food Composition and Analysis* 95: 103701. http://doi.org/10.1016/j.jfca.2020.103701.

Wadhera, R. K., D. L. Steen, I. Khan, R. P. Giugliano, and J. M. Foody. 2016. "A Review of Low-Density Lipoprotein Cholesterol, Treatment Strategies, and Its Impact on Cardiovascular Disease Morbidity and Mortality."

Journal of Clinical Lipidology 10, no. 3: 472–489. http://doi.org/10.1016/j.jacl.2015.11.010.

Walkowiak-Tomczak, D., J. Reguła, and A. Śmidowicz. 2018. "Effect of Prune *Prunus domestica* Consumption on Blood Lipid Profile in Patients With Moderate Hypercholesterolemia." *Acta Scientiarum Polonorum Hortorum Cultus* 6, no. 17: 17–25. http://doi.org/10.24326/asphc.2018.6.2.

Wallace, T. 2017. "Dried Plums, Prunes and Bone Health: A Comprehensive Review." *Nutrients* 9, no. 4: 401. https://doi.org/10.3390/nu9040401.

Wang, Y., X.-J. Liu, J.-B. Chen, J.-P. Cao, X. Li, and C.-D. Sun. 2022. "Citrus Flavonoids and Their Antioxidant Evaluation." *Critical Reviews in Food Science and Nutrition* 62, no. 14: 3833–3854. https://doi.org/10.1080/10408398.2020.1870035.

Watanabe, T., N. Nakaya, K. Kurashima, S. Kuriyama, Y. Tsubono, and I. Tsuji. 2004. "Constipation, Laxative Use and Risk of Colorectal Cancer: The Miyagi Cohort Study." *European Journal of Cancer* 40, no. 14: 2109–2115. http://doi.org/10.1016/j.ejca.2004.06.014.

Wesche-Ebeling, P., A. Argaíz-Jamet, L. G. Hernández-Porras, and A. López-Malo. 1996. "Preservation Factors and Processing Effects on Anthocyanin Pigments in Plums." *Food Chemistry* 57: 399–403. http://doi.org/10.1016/0308-8146(95)00240-5.

Xiao, Y. L., Y. Gong, Y. J. Qi, Z. M. Shao, and Y. Z. Jiang. 2024. "Effects of Dietary Intervention on Human Diseases: Molecular Mechanisms and Therapeutic Potential." *Signal Transduction and Targeted Therapy* 9, no. 1: 59. http://doi.org/10.1038/s41392-024-01771-x.

Youssef, F. S., M. L. Ashour, H. A. El-Beshbishy, A. Ahmed Hamza, A. N. B. Singab, and M. Wink. 2020. "Pinoresinol-4-*O-Beta*-D-Glucopyranoside: A Lignan From prunes (*Prunus domestica*) Attenuates Oxidative Stress, Hyperglycaemia and Hepatic Toxicity In Vitro and In Vivo." *Journal of Pharmacy and Pharmacology* 72, no. 12: 1830–1839. http://doi.org/10.1111/jphp.13358.

Youssef, F. S., E. T. Menze, and M. L. Ashour. 2020. "A Potent Lignan From prunes Alleviates Inflammation and Oxidative Stress in Lithium/Pilocarpine-Induced Epileptic Seizures in Rats." *Antioxidants (Basel)* 9, no. 7: 575. http://doi.org/10.3390/antiox9070575.

Zhang, J., X. Wang, V. Vikash, et al. 2016. "ROS and ROS-Mediated Cellular Signaling." *Oxidative Medicine and Cellular Longevity* 2016, no. 1: 4350965. http://doi.org/10.1155/2016/4350965.

Zhebentyayeva, T., V. Shankar, R. Scorza, et al. 2019. "Genetic Characterization of Worldwide *Prunus domestica* (Plum) Germplasm Using Sequence-Based Genotyping." *Horticulture Research* 6: 12. http://doi.org/10.1038/s41438-018-0090-6.

Zhu, K., and R. L. Prince. 2015. "Lifestyle and Osteoporosis." *Current Osteoporosis Reports* 13, no. 1: 52–59. http://doi.org/10.1007/s11914-014-0248-6.