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REVIEW

A Systematic Review on the Health Effects of Plums (*Prunus domestica* and *Prunus salicina*)

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In recent times, plums have been described as foods with health-promoting properties. Research on the health effects of plum continue to show promising results on its antiinflammatory, antioxidant and memory-improving characteristics. The increased interest in plum research has been attributed to its high phenolic content, mostly the anthocyanins, which are known to be natural antioxidants.

A systematic review of literature was carried out to summarize the available evidence on the impact of plums (*Prunus* species; *domestica* and *salicina)* on disease risk factors and health outcomes.

A number of databases were searched according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for relevant studies on plum health effects *in vitro*, animal studies and clinical trials.

A total of 73 relevant peer-reviewed journal articles were included in this review. The level of evidence remains low. Of the 25 human studies, 6 were confirmatory studies of moderate quality, while 19 were exploratory. Plums have been shown to possess antioxidant and antiallergic properties, and consumption is associated with improved cognitive function, bone health parameters and cardiovascular risk factors. Most of the human trials used the dried version of plums rather than fresh fruit, thus limiting translation to dietary messages of the positioning of plums in a healthy diet.

Evidence on the health effect of plums has not been extensively studied, and the available evidence needs further confirmation. Copyright © 2016 John Wiley & Sons, Ltd.

Keywords: plums; *Prunus domestica*; *Prunus salcina*; health effects; systematic review.

INTRODUCTION

The plum is a drupe fruit which belongs to the subgenus *Prunus* (Family Rosaceae). The subgenus can be differentiated from other subgenera (peaches, cherries, etc.) as the shoots have a terminal bud and unclustered single side buds, the flowers combine in groups of one to five on short stems, and the fruit have a crease running down one side and a smooth seed. Between 19 and 40 different species of plum exist. Of these, only 2, the hexaploid European plum (*Prunus domestica)* and the diploid Japanese plum (*Prunus salicina* and hybrids), are of commercial significance across the globe (Topp *et al*., 2012). The nutritional composition of the two species is considered similar (Table 1).

The European plum is believed to have been discovered about 2000 years ago, with its origin somewhere near the Caspian Sea. The fruit was introduced into the USA in the 17th century by pilgrims, while the Japanese plum has its origin in China but derived its name from the country where it was mostly cultivated and developed, Japan. The Japanese plum was introduced into the USA in the late 19th century. Today, the main producers of commercially grown plums are the United States, Serbia, China and Romania. (UN Food and Agriculture Organization, 2011).

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Prunes are the dried version of plums and are known for their laxative effect, which is commonly attributed to its high fibre content (Tinker *et al*., 1991). Earlier studies attributed the laxative effect of prunes to the presence of phenolics (chlorogenic acid) (Chok and Lang, 1961) and sorbitol (Reele and Chodos, 1985) that are in the fruit, together with its high fibre content (Stacewicz-Sapuntzakis *et al*., 2001). In the USA, prunes are referred to as dried plums. This name change was effected in a bid to promote prunes as a health food instead of being associated with old age (Zasky, 2008). Prunes are produced industrially by drying plums at 85–90°C for 18 h. This process is believed to have originated thousands of years ago also near the Caspian Sea, the same region where the European plums were discovered. With migration and civilization, prunes spread throughout Europe. Today, California, USA is the leading producer of prunes (dried plums) worldwide (Norton, 2009).

In classifying whole and natural foods based on their unique nutritional composition, flavonoid content is one of the most important methods of classification (Stadlmayr *et al*., 2011). The high levels of phenolic compounds, including flavonoids and particularly the subclass of anthocyanins observed in the plum, have resulted in a dramatically increased interest in plum-based research since the 1990s (Nakatani *et al*., 2000; Walle *et al*., 2003). A number of health benefits have been associated to the plum fruit and these include improved bone health, cognition and memory, antioxidant anti-inflammatory effects and easement of constipation.

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Table 1. Major nutritional composition of European (*Prunus domestica)* and Japanese (*Prunus salicina*) plums, per 100 g weight (data from (USDA, 2014); data are a mix of Japanese and European plums)

Component	European plum (*P. domestica) and* Japanese plums (*P. salicina*)		
	Fresh plums	Dried prunes	Plum juice
Water/moisture (g)	87.23	30.92	84.02
Energy (kj)	192	1006	243
Carbohydrate (g)	11.42	63.88	15.15
Protein (g)	0.70	2.18	0.51
Fat (g)	0.28	0.38	0.02
Sugars, total			14.22
Glucose (g)	5.07	25.46	23.3[a]
Fructose (g)	3.07	12.45	11.8[a]
Sucrose (g)	1.57	0.15	3.7[a]
Total dietary fibre	1.4	7.1	0.9
Minerals			
Calcium (mg)	6	43	10
Iron (mg)	0.17	0.93	0.34
Magnesium (mg)	7	41	8
Phosphorus (mg)	16	69	15
Potassium (mg)	157	732	154
Sodium (mg)	0	2	1
Zinc (mg)	0.10	0.44	0.11
Copper (mg)	0.057	0.281	0.054
Manganese (mg)	0.052	0.299	0.033
Fluoride (μg)	2.0	4.0	—
Vitamins			
Ascorbic acid (C) (mg)	9.5	0.6	2.8
Thiamine (B_1) (mg)	0.028	0.051	0.023
Riboflavin (B_2) (mg)	0.026	0.186	0.059
Niacin (B_3) (mg)	0.417	1.882	0.473
Pantothenic acid (B_5) (mg)	0.135	0.422	0.072
Pyridoxine (B_6) (mg)	0.029	0.205	0.027
Total Folate (μg)	5	4	3
Vitamin A, RAE (μg)	17	39	50
Vitamin E (mg)	0.26	0.43	0.18
Vitamin K_1 (μg)	6.4	59.5	4.3
Carotenoids			
Carotene, beta (μg)	190	394	554
Carotene, alpha (μg)	0	57	0
Cryptoxanthin, beta (μg)	35	93	102
Lutein + zeaxanthin (μg)	73	148	49
Phenolic compounds[b]			
Total (mg)	111	184	121[c]
Neochlorogenic acid (mg)	81	131	198.5[a]
Chlorogenic acid (mg)	14.4	44	46.5[a]
Anthocyanins (mg)	7.6	—	0.172[c]
Catechins (mg)	5.4	—	

Table adapted from (Stacewicz-Sapuntzakis, 2013) and (Netzel *et al.*, 2012)

[a](Stacewicz-Sapuntzakis, 2013) (plum juice concentrate)

[b](Mangels *et al.*, 1993)

[c](Shukitt-Hale *et al.*, 2009)

—No available data.

These health-promoting properties have been attributed to the plum's antioxidant capacity as a result of the high phenolic content (Yu *et al.*, 2009a; Noratto *et al.*, 2009; Franklin *et al.*, 2006; Pawlowski *et al.*, 2014; Shukitt-Hale *et al.*, 2009).

These observed health effects have been reported from studies that have used different research designs (*in vitro,* animal studies and clinical studies) and have investigated both plums, and related products and extracts (Stacewicz-Sapuntzakis, 2013).

The aim of this systematic literature review is to determine the level of current evidence on the beneficial health effects of plum and its associated products.

MATERIALS AND METHODS

A number of electronic databases were searched: Scopus, Web of Science, Cochrane library, CINAHL, MedLine and ScienceDirect up to June 2015 with a combination of search terms, including plum or prunes or *Prunus domestica or Prunus salicina* and health effects used as keywords (see Appendix 1 for Medline search strategy).

Inclusion criteria for journal articles include

1. Studies carried out *in vitro, on* animal and clinical studies.
2. Studies that utilized the fresh, dried, juice version or extracts of the plum species *P. domestica or P. salicina*.
3. All studies assessing any health outcome associated with plum consumption.
4. Studies reported in English. Only studies reported in English were included due to language barrier, reasons of time efficiency and cost of translation not being feasible.

Exclusion criteria for journal articles include

1. Studies on the quantification of the nutritional composition and antioxidant properties of plums.
2. Studies that utilize different species of plums, for example, the Japanese apricot, also known as Japanese plums in the *Prunus mume* specie.
3. Studies assessing properties related to plum cultivation, harvest and the commercial aspects of the plum fruit.

Articles were assessed for peer-reviewed status using Ulrich's Web (available at: http://ulrichsweb.serialssolutions.com.ezproxy.uow.edu.au/). A hand search yielded one additional article, which was relevant to this review.

For the clinical trials, all the relevant studies retrieved were classified as either confirmatory or exploratory studies. They were rated for their quality using relevant criteria from the Delphi list, Cochrane Back Review Group and the CONSORT Statement (Table 9), and strength of evidence of study design assessed using the Australian National Health and Medical Research Council hierarchy levels of evidence with rankings from level I–IV.

The National Health and Medical Research Council evidence hierarchy has six levels according to type of research question with systematic review of level II studies classified as levels I, randomized controlled trials, classified as level II. Studies ranging from a pseudorandomised

controlled trial to a comparative study without concurrent controls classified as levels III-1 to III-3 and case series with either post-test or pre-test/post-test outcomes classified as level IV (NHMRC, 2000).

RESULTS

A total of 73 studies were eligible for inclusion in this review (Fig.1). Of these, 18 investigated bone health (2 *in vitro,* 12 animal studies and 4 clinical trials), and 20 investigated its anticancer and antiinflammatory properties (13 *in vitro* studies, 6 animal studies and 1 clinical trial). Eleven studies reported on plums' antioxidant properties and their effect on cognition (2 *in vitro* studies, 5 animal studies and 4 clinical trials) while nine studies investigated the effect of plums on different components of the metabolic syndrome (cholesterol, high blood pressure and anti-thrombosis; 3 animal studies and 6 clinical trials). For its commonly known laxative effect and satiety, 8 clinical studies were carried out. Five studies examined its anti-allergic, anti-microbial and immune-enhancing properties (2 *in vitro* studies and 3 animal studies), and 2 clinical studies examined its effects on liver function and risk factors for kidney stone formation. Some of the findings reported from the *in vitro* studies like improved bone health and anti-inflammatory properties have also been confirmed in animal and human studies. Tables 2–8 summarize the experimental and clinical studies, and Table 9 summarizes the quality of the clinical studies included in this review.

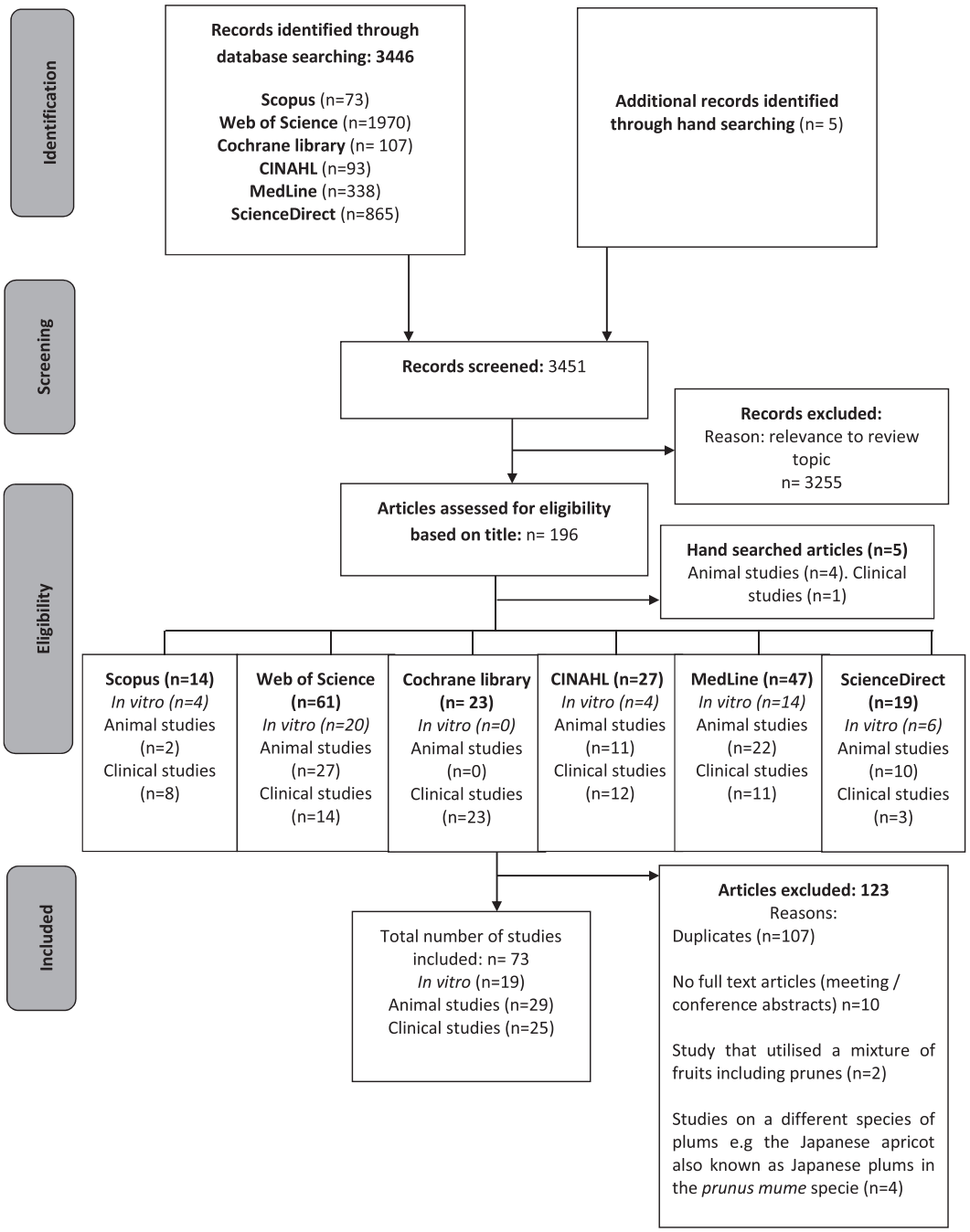

Figure 1. PRISMA flow diagram for study selection process.

Table 2. Evidence on the effect of plums and its associated products on bone health

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed
In vitro studies					
(Bu *et al.*, 2008)	USA	Dried plum extract (*Prunus domestica)*	RAW 264.7 murine macrophage cells		Inhibition of osteoclastogenesis under inflammatory and oxidative stress conditions possibly by polyphenol content
(Bu *et al.*, 2009)	USA	Polyphenols extracted from dried plum (*P. domestica)*	MC3T3-E1 cells pre-treated with dried plum polyphenols (0, 2.5, 5, 10 and 20 μg/mL) and 24 h later stimulated with TNF-α (0 or 1.0 ng/mL).		Improvement of osteoblast activity and function by up-regulating Runx2, Osterix and IGF-I and increasing lysyl oxidase expression, and reduction in osteoclastogenesis signalling
Animal studies					
(Smith *et al.*, 2014a)	USA	Dried plum (*P. domestica*)	Six weeks dietary supplementation of dried plum (5%, 15% or 25%) in adult, osteopenic ovariectomized rats		Restoration of bone mineral density by two higher doses and bone turnover suppression
(Deyhim *et al.*, 2005)	USA	Dried plum (*P. domestica)*	Dietary supplementation of dried plum (5%, 15% and 25%) in adult, osteopenic ovariectomized rats for 40 days		Bone quality improvement (restoring bone density) with all doses
(Franklin *et al.*, 2006)	USA	Dried plum (*P. domestica)*	Dietary supplementation of dried plum (5%, 15% and 25%) in orchidectomized rats for 90 days		Prevention of osteopenia in androgen deficient male rats
(Bu *et al.*, 2007)	USA	Dried plum (*P. domestica)*	Dietary supplementation of dried plum (25%) in osteopenic orchidectomized rats for 90 days		Reversion of bone loss due to orchidectomy
(Smith *et al.*, 2014b)	USA	Dried plum (*P. domestica)*	Dietary supplementation of dried plum (25%) in adult mice for 4 or 12 weeks		Improvement in bone mass and structure
(Rendina *et al.*, 2013)	USA	Dried plum (*P. domestica)*	Eight weeks dietary supplementation of dried plum (25%) in adult, osteopenic ovariectomized mice		Bone loss prevention with anabolic effect
(Halloran *et al.*, 2010)	USA	Dried plum (*P. domestica)*	Dietary supplementation of dried plum (15% or 25%) in adult and aged (old) male mice for 6 months		Restoration of lost bone and increase in bone volume
(Rendina *et al.*, 2012)	USA	Dried plum (*P. domestica)*	Dietary supplementation of dried plum (5%, 15% or 25%) in ovariectomized adult mice for 4 weeks		Improvement of bone structure and biomechanical properties and suppression of lymphocyte TNF-α production by higher doses
(Pawlowski *et al.*, 2014)	USA	Dried plum powder extract (*P. domestica)*	Dietary supplementation of plum extract (9% or 20%) in ovariectomized rats for six intervention (10 days) and washout (10 days) cycles		Improvement in bone calcium retention
(Monsefi *et al.*, 2013)	Iran	Plum extract (*P. domestica)*	Oral administration of plum extract (1.6 g/kg) in distilled water in pregnant mice for 30 days		Increased osteogenesis index in fetuses of mice treated with plum extract
(Arjmandi *et al.*, 2010)	USA	Dried plum (*P. domestica)*	One hundred eighty 3-month-old female Sprague–Dawley rats assigned to 15 groups (n = 12) and either ovariectomized (14 groups) or sham-operated (Sham, one group) then placed on different dietary treatments including one supplemented with 5% fructooligosaccharides and 7.5% dried plum for 60 days.		Diets supplemented with 5% fructooligosaccharides and 7.5% dried plum was most effective in reversing both right femur and fourth lumbar bone mineral density and fourth lumbar calcium loss while significantly decreasing trabecular separation.

(Continues)

Table 2. (Continued)

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed
(Johnson *et al.*, 2011)	USA	Dried plum (*P. domestica*)	Seventy two 3-month-old female Sprague–Dawley rats assigned to six groups (n = 12/group) and either ovariectomized (five groups) or sham-operated (Sham, one group) then placed on a semi purified, powdered casein-based diet for 45 days to induce bone loss. Thereafter, the groups were placed on different dietary treatments, including one supplemented with 5% fructooligosaccharides and 7.5% dried plum for 60 days.		In combination with soy protein, dried plum and fructooligosaccharides had the most pronounced effect in increasing lumbar bone mineral density.
Clinical trials					
(Hooshmand *et al.*, 2011)	USA	Dried plum (*P. domestica*)	Hypothesis: dried plums reverses bone loss in osteopenic postmenopausal women. n = 160 osteopenic postmenopausal women Study design/methods: randomized controlled trial. Postmenopausal women randomly assigned to treatment groups of dried plum (100 g/d) or dried apple (75 g) daily for 1 year. Blood and urine samples collected. Sample size power: not stated Dose: 100 g/day. Duration: 1 year.	II Confirmatory	Statistically significant increase in bone mineral density of ulna and spine with decreased serum levels in bone turnover markers (bone-specific alkaline phosphatase and tartrate-resistant acid phosphatase-5b) observed
(Arjmandi *et al.*, 2002)	USA	Dried plum (*P. domestica*)	Hypothesis: addition of dried plums to the diets of postmenopausal women would positively influence markers of bone turnover. n = 58 postmenopausal women Study design/methods: randomized controlled trial. Postmenopausal women randomly assigned to treatment groups of dried plum (100 g/d) or dried apple (75 g) daily for 3 months. Blood and urine samples collected. Sample size power: not stated Dose: 100 g/day. Duration: 3 months.	II Exploratory	Statistically significant increase in serum levels of insulin-like growth factor-1 and bone-specific alkaline phosphatase associated with increased rates of bone formation
(Hooshmand *et al.*, 2014)	USA	Dried plum (*P. domestica*)	Hypothesis: dried plum has an effect on circulating levels of sclerostin and bone metabolism measured in serum levels of receptor activator of NF-$_k$B ligand and osteopotegerin. n = 160 women with mild bone loss. Study design/methods: randomised controlled trial. Subjects randomly assigned to one of two groups of dried plum or dried apple and provided with	II Exploratory	Increase in bone mineral density of the ulna and spine and also the receptor activator of NF-$_k$B ligand and osteopotegerin levels. A reduction in serum sclerostin was also observed.

(Continues)

Table 2. (Continued)

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed
(Simonavice *et al.*, 2014)	USA	Dried plum (*P. domestica)*	500 mg Caplus 400 IU (10 μg) vitamin D. Sample size power: not stated Dose: 100 g dried plum per day Duration: 1 year Hypothesis: 6-month intervention with resistance training and a combination of resistance training and dried plum would improve total and regional (lumbar spine, femur and forearm) BMD. Increase lean body mass, skeletal muscular strength and decrease fat body mass. Additionally, it was hypothesized that the biochemical analyses for both groups would reveal increased levels of bone formation markers, decreased levels of bone resorption markers, and decreased levels of inflammation markers, with the RT + DP group having the most improvements in these areas in breast cancer survivors. n = 23 female breast cancer survivors. Study design/methods: case–control. Subjects stratified into 1(RT) or 2(RT + DP) treatment groups. Sample size power: not stated Dose: 90 g dried plum per day Duration: 6 months	II Exploratory	No difference between groups or any group-by-time interaction observed for any of the variables.

RT, resistance training; DP, dried plum.

*Clinical trials ranked using (NHMRC, 2000) Levels of Evidence Hierarchy where I is a systematic review (highest rating) and IV is a case series or cross-sectional study (lowest rating) and also classified as exploratory or confirmatory studies.

Table 3. Evidence on the anti-cancerous and antiinflammatory properties of plums and its associated products

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed
In vitro studies					
(Yu *et al.*, 2009a)	Korea	Immature plum extract (IPE) *(Prunus salicina)*	Human hepatocellular carcinoma HepG2 cells, Kato III gastric cancer cells, HeLa human cervical carcinoma cells, U937 leukaemia cells and MCF 7 hormone-dependent breast cancer cells		Cell growth inhibition by IPE, that is, induction of cancerous cell apoptosis
(Noratto *et al.*, 2009)	USA	Mature red-fleshed plum extract (*Prunus domestica)*	MCF-7; the oestrogen-positive human breast cancer cell line, MDA-MB-453; the oestrogen negative human breast cancer cell line, and MCF-10A; the breast epithelial cells		Inhibition of breast cancer cell proliferation and significantly reduced toxicity on the normal cells
(Lee *et al.*, 2009)	USA	Plum extract *(P. salicina)*	Chicken spleen, RP9 tumour cells and HD11 macrophages		Stimulation of spleen lymphocyte proliferation and NO production by cultured macrophages and inhibition of tumour cell growth
(Fujii *et al.*, 2006)	Japan	Prune extract (*P. domestica)*	Caco-2 human colon carcinoma cell line, KATO III human stomach carcinoma cell line and CCD-18Co normal human colon fibroblast cell line		Induction of cell apoptosis of cancer cells but not normal cells
(Lea *et al.*, 2008)	USA	Plum extract (*P. domestica)*	SW1116, HT29, Caco-2 human colon cancer cells and NCM460 human colon cells.		Growth inhibition and induction of differentiation on colon cancer cells
(Hooshmand *et al.*, 2015)	USA	Dried plum polyphenol extract (*P. domestica)*	Stimulation of macrophage RAW 264.7 cells with either 1 $\mu g\ mL^{-1}$ (for measurement of NO production) or 1 $ng\ mL^{-1}$ (for measurement of COX-2 expression) of lipopolysaccharide to induce inflammation and treated with different doses of dried plum polyphenols.		Reduction in Nitric oxide and malondialdehyde production with highest dose treatment (1000 $\mu g\ mL^{-1}$). Reduction in lipopolysaccharide-induced expression of COX-2 by the 100 and 1000 $\mu g\ mL^{-1}$ dose.
(Kim *et al.*, 2003)	USA	Plum polyphenol extract (*P. domestica)*	Treatment of two cancer cell lines (HepG2 human liver cancer cells and DLD1 human colon cancer cells) with polyphenol extract of plum.		Antiproliferative activities on both cancer cell lines in a dose dependent manner.
(Nishida *et al.*, 2014)	Japan	Plum pectin extract (*P. domestica)*	Incubation of heparan sulfate in differentiated Caco-2 cells with pectin extracted from plums.		There was an obvious change in the sulphated structures of HS following pectin administration. Also, pectin upregulated human HS 6-O-endosulfatase-2 (HSulf-2) expression and inhibited HSulf-1 expression.
(Nishida *et al.*, 2015)	Japan	Plum pectin extract (*P. domestica)*	Incubation of differentiated Caco-2 cells (cultured in 6-well plates at a cell density of 1.0×10^5 cells/well), with pectin, extracted from plums.		Pectin-treated differentiated Caco-2 cells promoted growth of IEC-6 cells and also an upregulation of relative mRNA and protein expression levels of Wnt3a protein.

(Continues)

Table 3. (Continued)

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed
(Popov *et al.*, 2014)	Russia	Plum pectic polysaccharide extract (*P. domestica)*	0.05 mL of plum pectic polysaccharide added to peritoneal cell suspension and incubated in a 96-well flat-bottom tissue culture plate in the absence or presence of phorbol-12-myristate-13-acetate at 37°C for 15 mins.		Reduction in the adhesion of peritoneal leukocytes. Inhibition of the production of superoxide anion radicals by reducing xanthine oxidase activity.
(Vizzotto *et al.*, 2014)	USA	Plum polyphenol extract (*P. domestica)*	Oestrogen independent MDA-MB-435, oestrogen dependent MCF-7 breast cancer cell lines and one non-cancerous breast line MCF-10A exposed to varying concentrations of plum extracts for 24 h.		Dose-dependent cytotoxic effect against MDA-MB-435, weak activity against MCF-7 and small or no activity against MCF-10A observed.
(Yu *et al.*, 2007)	Korea	Immature, mid-mature and mature plum extract *(P. salicina)*	Six human cell cancer lines (Hep G2 human hepatocellular carcinoma cells and Kato 111 human gastric carcinoma cells, Hela human cervical carcinoma cells, U937 human leukaemia cells, MCF 7 hormone-dependent human breast cancer cells, and MDA-MB-231 hormone-independent human breast cancer cells) incubated with varying concentration of plum extract.		Cytotoxic effects observed and apoptosis observed in MDA-MB-231 cells mediated by the immature plum extract.
(Yu *et al.*, 2009b)	Korea	Immature plum extract *(P. salicina)*	Incubation of PMA-induced HepG2 human hepatocellular carcinoma cells with Immature plum extract.		Antimigrative property in (phorbol 12-myristate 13-acetate) PMA-induced HepG2 cells observed. A strong inhibitory effect on the PMA-induced MMP-9 secretion through suppression of the transcriptional activity of the MMP-9 gene independently of the TIMP gene in HepG2 cells was also observed.
Animal studies					
(Kim *et al.*, 2008)	Korea	Immature plum extract IPE *(P. salicina)*	Intraperitoneal injection of IPE (2.5 or 5 g/kg bw/day) dissolved in phosphate buffered saline for 5 days in male mice with benzo(α)pyrene induced liver toxicity		Chemopreventive efficacy by inhibiting the induction of CYP1A1 expression and reducing the activity of glutathione peroxidase, superoxide dismutase and catalase
(Cantu-Jungles *et al.*, 2014)	Brazil	Polysaccharides from prunes (*P. domestica)*	Inducement of acute gastric ulcer in rats using intragastric administration of ethanol P.A. after four different oral treatments including polysaccharides from prunes fraction (3 and 10 mg/kg).		Reduction and inhibition of gastric lesion area by prune polysaccharides fractions.
(Noratto *et al.*, 2015)	USA	Plum juice *(P. salicina)*	Administration of plum juice in drinking water to obese Zucker rats *ad libitum* for 11 weeks		Antiadipogenic and anti-inflammatory effects. Reduction in blood glucose, triglycerides and HDL cholesterol levels

(Continues)

Table 3. (Continued)

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed
(Mishra *et al.*, 2012)	India	Plum extract (*P. domestica)*	Inducement of peptic ulcer by pyloric ligation in Wistar albino rats after administration of plum extract (100, 150 or 200 mg kg^{-1}) for 7 days		Antioxidant and anti-ulcerogenic activity
(Yang and Gallaher, 2005)	USA	Dried plum (*P. domestica)*	Dietary supplementation of dried plum (4.75 or 9.5%) in male Wistar rats for 10 days followed by administration of two doses (1 week apart) of azoxymethane and dietary supplementation for 9 more weeks		Inhibition of risk factors associated with colon carcinogenesis (reduction in faecal total and secondary bile acids concentration, reduction in colonic β-glucuronidase and 7α-dehydroxylase activities and increased antioxidant activity)
(Gallaher and Gallaher, 2009)	USA	Dried plum (*P. domestica)*	Dietary supplementation of dried plum (4.75 or 9.5%) and cholesterol in apolipoprotein E-deficient mice for 5 months.		Development of atherosclerosis Impeded
Clinical trial					
(Kasim-Karakas *et al.*, 2002)	USA	Dried plum (*P. domestica)*	Hypothesis: prune intake may alter the metabolism of estrogens because prunes are a rich source of both soluble and insoluble fibre and cinnamates and decrease intestinal transit time. *n* = 19 healthy premenopausal women Study design/methods: crossover study. After consuming habitual diets for three menstrual cycles (control run-in period), participants replaced dietary simple sugars with prunes for another three menstrual cycles (intervention period). Sample size power: not stated Dose: 100 g dried plum per day Duration: 6 months.	III-2 Exploratory	Decrease in the independent excretion of 2OHE1 and 16αOHE1 observed but no statistically significant change in the 2OHE1 - 16αOHE1 ratio following prune supplementation

*Clinical trials ranked using (NHMRC, 2000) Levels of Evidence Hierarchy where I is a systematic review (highest rating) and IV is a case series or cross-sectional study (lowest rating) and also classified as exploratory or confirmatory studies.

Table 4. Evidence on the antioxidant property and effect on cognition of plums and its associated products

Reference	Location	Plum product investigated	Sample/method	Level of evidence	Effects observed
In vitro studies					
(Bouayed *et al.*, 2009)	France	Phenolics from plums (*P. domestica)*	Polyphenolics extracted from seven varieties of plum and quantified. Their antiradical activities and protection against oxidative stress evaluated in peripheral blood granulocytes.		Antioxidant activity and protection of blood granulocytes from H_2O_2-induced oxidative stress by preventing granulocytes from intracellular ROS accumulation.
(Donovan *et al.*, 1998)	USA	Prune/prune juice extract (*P domestica)*	Human LDL from plasma prepared from blood collected from healthy volunteers.		Inhibition of LDL oxidation.
Animal studies					
(Shukitt-Hale *et al.*, 2009)	USA	Plum juice/dried plum powder (*P. domestica)*	Two groups of aged rats with either consumption of a mixture of water and plum juice (100%) (Group 1) or dietary supplementation with dried plum powder (2%) (group 2) for 8 weeks		Improved cognitive function assessed by Morris Water Maze
(Shahidi *et al.*, 2013)	Iran	Plum extract (*P. domestica)*	Plum extracts (75, 100, 150 mg/kg) administration by oral gavage to male mice once a day for 7 days		Improvement in learning and memory in mice assessed by the passive avoidance test
(Kao-Ting *et al.*, 2013)	Taiwan	Dried plum powder *(Prunus salicina)*	Dietary supplementation of dried plum powder (2%) in nicotinamide/streptozotocin-induced diabetic rats for 2 months		Improvement in cognitive performance, antioxidant activity and improvement in insulin sensitivity
(Sharma and Sisodia, 2013)	India	Plum extract (*P. domestica)*	Administration of optimum dose of plum extract in distilled water to mice for 15 days pre/post whole body exposure to 10 Gy gamma-radiations		Antioxidant capabilities and improved spatial learning
(Bouayed *et al.*, 2007)	France	Chlorogenic acid from *P. domestica*	Administration of chlorogenic acid (20 mg/kg) to mice and antioxidant effect on peripheral blood granulocytes.		Decrease in anxiety related behaviours (anxiolytic-like effect) and protection of granulocytes from oxidative stress by chlorogenic acid *in vitro.*
Clinical trials					
(Prior *et al.*, 2007)	USA	Dried plum/ dried plum juice (*P. domestica)*	Hypothesis: changes in antioxidant capacity following consumption of plum juice may be used to assess its potential to alter *in vivo* antioxidant status and provide estimates of dietary antioxidants necessary to prevent postprandial oxidative stress. n = 6 healthy volunteers. Study design/methods: randomized cross-over study. Fasting blood sample collected and participants fed test juices and blood samples	II Exploratory	No effect on plasma hydrophilic (H-) or lipophilic (L-) antioxidant capacity measured as Oxygen Radical Absorbance Capacity ($ORAC_{FL}$)

(Continues)

Table 4. (Continued)

Reference	Location	Plum product investigated	Sample/method	Level of evidence	Effects observed
			collected at 1, 2 and 4 h post juice consumption. Sample size power: not stated Dose: 315 mL of dried plum juice; or dried plums (131 g blended in 315 mL water Duration: 2 weeks (with 2 weeks washout period)		
(Ko *et al.*, 2005)	Korea	Plum juice *(P. salicina)*	Hypothesis: Consumption of fruit juices could scavenge ROS generated in human plasma. *n* = 10 healthy men. Study design/methods: cross-over study. Consumption of single dose of 150 mL of plum juice. Blood samples collected at 0, 30, 60, 90 and 120 min after consumption Sample size power: not stated Dose: a single dose of 150 mL Duration: 1 day (with 1 day washout period)	IV Exploratory	Improved antioxidant activity in human plasma measured by dichlorofluorescein fluorescence
(González-Flores *et al.*, 2011)	Spain	Plum *(P. salicina)*	Hypothesis: there is a possible antioxidant effect associated with diets enriched with Japanese plums (*P. salicina* Lindl. cv. Crimson Globe) in young, middle-aged and elderly individuals. *n* = 18 (6 per young, middle aged and older group). Study design/methods: Consumption of 390 g plums without seeds per day divided into two portions: 195 g as the lunch dessert and 195 g as the dinner dessert for 5 days. First-void morning urines were collected before treatment (basal values), the immediate day after the last ingestion of plums (assay) and 1 day afterwards (post-assay). Sample size power: not stated Dose: 2 portions 390 g (195 g each) daily. Duration: 5 days.	IV Exploratory	Statistically significant increase in antioxidant capacity and urinary 6-sulfatoxymelatonin (aMT6-s)

(Continues)

Table 4. (Continued)

Reference	Location	Plum product investigated	Sample/method	Level of evidence	Effects observed
(Netzel *et al.*, 2012)	Australia	Plum juice *(P. salicina)*	Hypothesis: there is a possible antioxidant effect associated with Queen Garnet Plum Juice ingestion on the urinary antioxidant capacity and the concentration of malondialdehyde, a biomarker for oxidative stress. n = 2 healthy male subjects Study design/methods: crossover study. Consumption of 400 mL of Queen Garnet Plum Juice or 400 mL of water as an antioxidant-free control beverage separated by a 1-week washout phase. Sample size power: not stated Dose: single dose of 400 mL.	IV Exploratory	Increase in urinary antioxidant capacity and decrease in malondialdehyde excretion (biomarker for oxidative stress)

LDL, low-density lipoprotein; ROS, reactive oxygen species.

Table 5. Evidence on the effect of plums and its associated products on the different components of metabolic syndrome

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed/conclusion
Animal studies					
(Negishi *et al.*, 2007)	Japan	Prune extract (*Prunus domestica)*	Dietary supplementation of prune extract (25%) in stroke-prone spontaneously hypertensive rats for 5 weeks		Suppression of high (systolic) blood pressure
(Kuo *et al.*, 2015)	Taiwan	Plum powder *(Prunus salicina)*	Dietary supplementation of plum powder (2% or 5%) in high cholesterol diet in mice for 5 months		Amelioration of some symptoms of neurodegenerative conditions like increased cholesterol and β-amyloid (Aβ) concentration in the brain by both doses
(Lucas *et al.*, 2000)	USA	Dried plums (*P. domestica)*	Dietary supplementation (5% or 25% dried plum) with dried plum in 48 ovariectomized (ovx) 90-day old female Sprague–Dawley rats for 45 days.		With elevated serum total cholesterol brought about by ovariectomy, 25% prune diet prevented this increase without affecting HDL cholesterol concentration and also reduction in liver total lipids was observed.
Clinical trials					
(Tinker *et al.*, 1991)	USA	Dried plums (*P. domestica)*	Hypothesis: (a) prunes as a source of fibre can lower plasma cholesterol in men with mild to moderate hypercholesterolemia (5.2–7.5 mmol cholesterol/L). (b) faecal bile acid excretion is increased in response to the ingestion of prunes as a source of fibre, which may help explain the cholesterol lowering effect of fibre. *n* = 41 free living men with mild hypercholesterolemia. Study design/methods: crossover study. 8 weeks period split into two experimental diet periods, each lasting 4 weeks. Subjects randomly assigned a diet sequence, starting with either consumption of a grape juice-control supplement (GJ control) or a prune supplement. Sample size power: not stated Dose: 12 prunes *(*~100 g/d) Duration: 8 weeks.	II Confirmatory	Plasma LDL cholesterol was statistically significantly reduced after the prune period than the control, faecal bile acid conc. of lithocholic acid was also statistically significantly lower with prune consumption and both faecal wet and dry weights were statistically significantly higher with prune consumption.
(Chai *et al.*, 2012)	USA	Dried plums (*P. domestica)*	Hypothesis: regular intake of apple favourably improves lipid profiles, reduces atherogenic risk ratios, lowers C-reactive protein levels, and decreases levels of oxidative stress marker in postmenopausal women *n* = 160 postmenopausal women Study design/methods: case–control study. Subjects randomly assigned to treatment groups of dried apple (75 g) or dried plum (100 g/d)	II Exploratory	No statistically significant difference between treatment groups in altering serum levels of atherogenic cholesterols observed. For the dried apple group, total cholesterol was statistically significantly reduced at 6 months.

(Continues)

Table 5. (Continued)

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed/conclusion
			Sample size power: 95% Dose: 100 g/day Duration: 1 year.		
(Afaghi *et al.*, 2009)	Iran	Prunes	Hypothesis: 8 fruits (Golab apples, green apples, fresh apricots, prunes, cherries, blueberries, golden no-seed grapes, and red sultanas) are low glycemic index and recommendable for diabetics and weight loss. $n = 8$ Study design/methods: crossover study. Eight subjects (healthy, young men aged 20–28, normal weight with body mass index: 20–25 kg/m^2) randomly assigned to one of eight fruits and blood glucose measured at 0, 15, 30, 45,60, 90 and 120 mins after consumption. Sample size power: 95% Dose: 143 g Duration: not stated — different occasions after overnight fasting.	II Exploratory	Serving size of prunes was low glycemic load fruit. Prunes among other tested fruits were low glycemic index and can be recommended for diabetics and weight loss management.
(Ahmed *et al.*, 2010a)	Pakistan	Prunes (*P. domestica)*	Hypothesis: use of prunes is useful in cardiovascular disorders to bring about changes in blood pressure or prevention of atherosclerosis. $n = 259$ pre-hypertensive patients (systolic BP = 120–139 mmHg, diastolic BP = 80–89 mmHg) Study design/methods: randomised controlled trial. Patients randomly assigned to three groups of A-single dose, B-double dose or C-control group. Blood pressure was recorded fortnightly, and blood samples were taken at 0 and 8 weeks. Sample size power: not stated. Dose: group A-11.5 gm. Group B-23 gm. Control-glass of water. Duration: 8 weeks.	II Confirmatory	Reduction of blood pressure by single dose of prunes daily group and the controls with the double dose of prunes showing a reduction in just systolic blood pressure. There was an increase in serum HDL of the control group whereas test groups had significantly reduced serum cholesterol and LDL. The data predicts cardiovascular protective effects of prunes.
(Santhakumar *et al.*, 2015a)	Australia	Plum juice *(P. salicina)*	Hypothesis: anthocyanin-rich Queen Garnet Plum Juice may ameliorate platelet activation-related thrombogenesis and maintain haemostatic function by (1) reducing platelet aggregation and activation through blocking/inhibiting various platelet activation pathways; (2) prolonging clotting time and reducing	II Exploratory	Queen Garnet Plum Juice supplementation inhibited platelet aggregation induced by adenosine diphosphate, collagen and arachidonic acid. There was reduction in platelet activation-dependent surface-marker P-selectin expression of activated de-granulated platelets. Increase in activated partial thromboplastin clotting time and reduction in plasma-

(Continues)

Table 5. (Continued)

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed/conclusion
			fibrinogen concentration; and (3) exhibiting favourable effects on lipid profile and inflammation. *n* = 21 Study design/methods: randomized, double blind, placebo crossover trial. Healthy volunteers randomly assigned to three supplement groups of A-Queen Garnet plum juice, B-prune juice or C-colour matched placebo. Blood samples were collected at least 8 h pre-prandial and mid-stream fasting urine samples collected. Sample size power: not stated. Dose: 200 mL/day of each juice. Duration: 28 days with 2 weeks washout period.		fibrinogen and malondialdehyde levels, a plasma biomarker of oxidative stress.
(Santhakumar *et al.*, 2015b)	Australia	Plum juice *(P. salicina)*	Hypothesis: anthocyanin-rich Queen Garnet Plum Juice may impart anti-thrombotic effects via (a) inhibition of platelet aggregation by simultaneously targeting different platelet activation pathways (adenosine diphosphate: ADP-P2Y12/P2Y1; collagen: GPVI/α2β1 and arachidonic acid: cyclooxygenase-1–COX-1), (b) reducing platelet hyper-activation and de-granulation by blocking surface receptors responsible for activation, and (c) favourably altering coagulation parameters and lipid profile. *n* = 13 Study design/methods: randomized, double blind, placebo crossover trial. Healthy volunteers randomly assigned to two supplement groups of A-Queen Garnet plum juice or B-a flavoured and coloured formulated cordial placebo. Oxidative stress was induced by constant load exercise bout for 1 h at 70% of their VO_{2PEAK} Blood samples were collected at fasting state and at least 8–12 h pre-prandial on day 1 and day 29.	II Exploratory	Inhibition of adenosine diphosphate-induced platelet aggregation both without and under exercise induced oxidative stress, inhibition of arachidonic acid-induced aggregation under oxidative stress. Also, there was reduced platelet activation-dependant P-selectin expression both without and under oxidative stress. Favourable effects on coagulation parameters both with and without oxidative stress were also observed.

(Continues)

Table 5. (Continued)

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed/conclusion
			Sample size power: not stated. Dose: 200 mL/day of each juice. Duration: 28 days with 2 weeks washout period.		

LDL, low-density lipoprotein; HDL, high-density lipoprotein.
*Clinical trials ranked using (NHMRC, 2000) Levels of Evidence Hierarchy where I is a systematic review (highest rating) and IV is a case series or cross-sectional study (lowest rating) and also classified as exploratory or confirmatory studies.

The quality of the clinical studies included is, at best, of moderate quality. There were 6 confirmatory studies of moderate quality (1 on bone health, 2 on different components of metabolic syndrome, and 3 on satiety and laxative effect) and 19 exploratory studies. Evidence on the health effect of plums has not been extensively studied, and the available evidence needs further confirmation.

BONE HEALTH

Based on results from 18 studies (2 *in vitro,* 12 animal studies and 4 clinical trials) reported in this review, promising evidence exists on the effect of plum on bone health. This body of evidence has mostly been in agreement and also confirmed in human trials. Bu *et al.* (2008) in their *in vitro* study involving two groups investigated the effect of dried plum polyphenols on osteoclastogenesis in which one group was stimulated with lipopolysaccharide (LPS) to induce inflammation and the other group stimulated with hydrogen peroxide (H_2O_2) to induce lipid peroxidation. It was observed that the LPS-stimulated sample produced NO (nitric oxide) detectable at 8 h, which further increased at 16 h, while the H_2O_2 stimulated cells did not produce NO. This increase in NO associated with LPS was downregulated by different doses (10, 20, 30 μg/mL) of plum polyphenol at both 8 h and 16 h. The authors concluded that dried plum polyphenols directly inhibit osteoclastogenesis, which leads to reduced osteoclast activity by downregulation of Nuclear factor of activated T-cells, cytoplasmic 1 (NFATc1) and inflammatory mediators.

The results from this *in vitro* experiment by Bu *et al.* (2008) has also been confirmed in animal studies (Deyhim *et al.*, 2005; Franklin *et al.*, 2006; Bu *et al.*, 2007; Smith *et al.*, 2014a). Among these, the study by Smith *et al.* (2014a) is slightly different in that unlike the other studies that studied longer term effects of dried plum on systemic biochemical markers of bone metabolism and alteration in gene expression as the main outcome measure, their main objective was to understand the mechanism of action by which dried plum altered bone metabolism. Regulators of osteoblast and osteoclast differentiation and osteoblast activity were studied over a period of 6 weeks. Compared with the anabolic therapy using parathyroid hormone that significantly increased systemic and local indicators of bone formation with no effect on systemic marker of bone resorption, dried plum supplementation suppressed bone turnover with no effect on the indices of bone formation at the endocortical surface. In another study by the same research team, dried plum supplementation initially suppressed cancellous bone turnover but demonstrated a biphasic response over time, exerting positive effects on bone mass and bone structure (Smith *et al.*, 2014b). Plum extract has also been shown to be effective in increasing bone calcium retention by 20% (Pawlowski *et al.*, 2014).

Rendina *et al.* (2013) compared the dried plum with other dried fruits (apple, apricot, grape and mango) and observed that only the dried plum had an anabolic effect on trabecular bone in the vertebra and prevented bone loss in the tibia. This demonstrates a potentially unique effect of plum that was absent in the other fruits

Table 6. Evidence on the satiety and laxative effect of plums and its associated products

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed
Clinical trials					
(Piirainen *et al.*, 2007)	Finland	Prune juice (prepared from plum juice concentrate, prune puree, water and 7% fructose) (*Prunus domestica)*	Hypothesis: prune juice alone may have a laxative effect on the bowel function of those adults with certain gastrointestinal symptoms but are otherwise healthy. *n* = 54 volunteers with mild GIT symptoms. Study design/methods: 1 week baseline period, 2 week prune juice (consumption) period followed by 1 week follow-up period with daily record of bowel habit Sample size power: not stated. Dose: 125 mL twice a day. Duration: 4 weeks.	IV Confirmatory	Laxative effect with increased flatulence.
(Cheskin *et al.*, 2009)	USA	Plum juice (*P. domestica)*	Hypothesis: plum juice supplementation diet would induce significant improvements in bowel frequency, and consistency, and possibly decrease appetite compared with baseline as well as placebo and psyllium treatments. *n* = 36 adults with chronic constipation symptoms. Study design/methods: randomized controlled crossover trial. Consumption of a daily portion of plum juice in comparison with psyllium and apple juice in adults with chronic constipation symptoms. Sample size power: not stated. Dose: 8 oz (237 mL) per day. Duration: 14 days.	II Confirmatory	Constipation relief and stool softening evident with consumption of plum juice.
(Attaluri *et al.*, 2011)	USA	Dried plum (*P. domestica)*	Hypothesis: dried plums are as effective as psyllium in the treatment of adults with chronic constipation. *n* = 40 patients with chronic constipation. Study design/methods: single blind, randomized cross-over study. Consumption of a daily portion of dried plums or psyllium for a treatment period of 3 weeks after which participants continued on their usual remedies for constipation for another 6 weeks. For the	II Confirmatory	Effective treatment with dried plum on mild to moderate constipation observed.

(Continues)

Table 6. (Continued)

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed
			duration of the study, subjects maintained daily symptom and stool diaries. Sample size power: 80%. Dose: 50 g twice a day with meals. Duration: 14 weeks (with 1 week washout period between treatments).		
(Farajian *et al.*, 2010)	Greece	Prunes (*P. domestica)*	Hypothesis: a preload including dried prunes consumed as a snack before a meal, compared with an isoenergetic bread product preload, would reduce (a) meal time energy intake, (b) appetite for dessert offered after lunch and, (c) energy intake for the next 24 h. *n* = 45 normal weight subjects. Study design/methods: randomized cross-over study. Fasting participants offered a standardized breakfast followed by a preload of either dried prunes or bread product after 2 h. Three hours after the preload, a standardized lunch and desert was provided. Subjects also rated their hunger, thirst, desire to eat, motivation to eat and satiety on 100 mm line visual analogue scales just before and right after the preload consumption, every 45 min up till the 180th minute On completion of the test day, detailed record of all foods and beverages intake for the next 24 h was collected. Sample size power: not stated. Dose: five prunes (40 g) before meals on each testing day. Duration: 2 days (with 1 week washout period).	II Exploratory	Reduced consumption of dessert with lower energy intake observed. An increased satiety at all time points between snack and meal was also observed.
(Furchner-Evanson *et al.*, 2010)	USA	Dried plum (*P. domestica)*	Hypothesis: snack choices similar in fat, protein, carbohydrate and sugar contents while differing in fibre content have an effect on satiety, subsequent food intake and plasma glucose, insulin and ghrelin responses. *n* = 19 healthy female subjects Study design/methods: randomized crossover study with at least 1 day washout. Subjects randomly assigned to receive four different test foods including dried plums. Blood samples	II Exploratory	Satiety index area under the curve greater for dried plum trial. Consumption of the dried plum elicited lower plasma glucose and insulin area under the curve and tended to promote a greater plasma ghrelin antioxidant capacity.

(Continues)

Table 6. (Continued)

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed
			collected at baseline and every 15 mins in 1 h then 90 and 120 mins. Sample size power: not stated. Dose: served in a 238 kcal (1000 kj) portion. Duration: not stated.		
(Howarth *et al.*, 2010)	USA	Dried plum (*P. domestica)*	Hypothesis: snack selection (dried plums vs common carbohydrate-rich low-fat cookies) influences daily energy consumption, nutrient intake and metabolic responses. *n* = 26 healthy female subjects Study design/methods: randomized crossover study with 2 weeks washout. Subjects randomly assigned to receive either dried plums or low-fat cookies for two separate 2-week feeding. A 7 day bowel habit questionnaire was completed. Sample size power: 80% Dose: served in a 100 kcal portion twice a day. Duration: 4 weeks.	II Exploratory	No change observed with energy intake or weight. In comparison with cookie, dried plum promoted greater intake of fibre, potassium, riboflavin, niacin and calcium. There was an observed reduction in total fat as well as cholesterol intake with dried plum snacks. Dried plum did not alter plasma triglyceride concentration but softer stool consistency was observed with dried plum consumption.
(Lucas *et al.*, 2004)	USA	Dried plum (*P. domestica)*	Hypothesis: dradual incorporation of 100 g of dried plum into the daily diet of healthy postmenopausal women would not cause significant changes in self-reported bowel habits including frequency of defecation, faecal bulk and stool consistency. *n* = 58 Study design/methods: randomized controlled trial. Postmenopausal women randomly assigned to treatment groups of dried plum (100 g/d) or dried apple (75 g) daily for 3 months. A 7 day bowel habit questionnaire was completed. Sample size power: not stated Dose: 100 g/day. Duration: 3 months.	II Exploratory	With both dried plum and apples, there was no statistically significant differences observed for any of the parameters used to assess bowel function. This indicates the absence of any negative side effects associated with prune consumption.
(Pasalar *et al.*, 2013)	Iran	Prunes (*P. Domestica)*	Hypothesis: prunes and flixweed are effective in the prevention of constipation among Iranian pilgrims who attended the Hajj ceremony in 2010 in the kingdom of Saudi Arabia.	II Exploratory	Using Rome III criteria to define constipation (less than three times of defecation/week, with straining, difficulty in defecation, unproductive urges, feeling

(Continues)

Table 6. (Continued)

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed
			Study design/methods: randomised controlled trial. 170 Iranian Hajj pilgrims randomly assigned to two groups of case and control. Case group received measured doses of prunes and flixweed daily before lunch and dinner and control group had their meals with no intervention. Sample size power: not stated Dose: 40–50 g/day with 10–15 g of flixweed. Duration: 3 weeks.		of anorectal obstruction, hand manoeuver to facilitate stool extraction and feeling of incomplete evacuation), a statistically significant difference was observed between the groups with the case group less constipated.

*Clinical trials ranked using (NHMRC, 2000) Levels of Evidence Hierarchy where I is a systematic review (highest rating) and IV is a case series or cross-sectional study (lowest rating) and also classified as exploratory or confirmatory studies.

Table 7. Evidence on the anti-allergic, anti-microbial and immune-enhancing property of plums and its associated products

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed
In vitro studies					
(Cevallos-Casals *et al.*, 2006)	USA	Plum extract (*Prunus salicina*)	Plum extract placed in a well with diluted bacteria inoculum.		Inhibitory effects against *Escherichia coli* 0157:H7 and *Samonella enteritidis.*
(Yaqeen *et al.*, 2013)	Pakistan	Prune extract (*Prunus domestica)*	Ethanol extracts of prunes tested against nine bacteria; five gram-positive bacteria (*Staphylococcus aureus*, *Streptococcuc intermedias*, *Bacillus cereus*, and *Bacillus pumilus*) and four gram-negative bacteria (*Eschrichia coli*, *Proteus mirabilis*, *Shigella flexneri*, *Salmonella typhi* and *Klebsiela pneumoniae*).		Antibacterial activity observed.
Animal studies					
(Karasawa *et al.*, 2012)	Japan	Prune extract (*P. salicina*)	Dietary supplementation with 25% ovalbumin and 1% prune extract over 6 weeks in rats injected 20 L of distilled water containing 20 g of mite allergen between the 3rd to 6th week		Reduction in allergic response in comparison with control group
(Lee *et al.*, 2008)	USA	Plum powder (*P. salicina*)	Dietary supplementation with 0.5% or 1.0% plum in 1-day old chickens and oral inoculation with 5000 sporulated oocysts of *Eimeria acervulina* at day 12 post-hatch.		Increase in body weight gain, levels of MRNAs for interferon-ϒ and interleukin-15. There was a reduction in faecal oocyst shedding and chickens fed the plum supplemented diets exhibited greater spleen cell proliferation
(Noratto *et al.*, 2014)	USA	Plum juice (*P. domestica)*	Administration of plum juice in obese Zucker rats for 11 weeks. Body weight recorded once a week.		Several bacteria groups (e.g. *Lactobacillus* and members of *Ruminococcacea*) were found to be more abundant in the plum group. There was also a distinct contrast between the microbiota of control and treatment groups.

*Clinical trials ranked using (NHMRC, 2000) Levels of Evidence Hierarchy where I is a systematic review (highest rating) and IV is a case series or cross-sectional study (lowest rating) and also classified as exploratory or confirmatory studies.

Table 8. Evidence on the effect of plum and its associated products on liver function and kidney stone risk factors

Reference	Location	Plum product investigated	Sample/method	Level of evidence*	Effects observed
Clinical trials					
(Ahmed *et al.*, 2010b)	Pakistan	Prune juice (*Prunus domestica)*	Hypothesis: prune juice does not alter liver function. *n* = 107 healthy volunteers Study design/methods: case–control study. Participants randomly assigned to three different groups of A (single dose of 1 pack of prunes = 11.43 kg, i.e. three prunes), B (control; a glass of water) and C (double dose of group A) consumed daily. Blood samples were taken on week zero and week 8 for liver function tests, that is, serum alkaline phosphatase, bilirubin, aspartate transaminase and alanine transaminase. Sample size power: not stated Dose: three prunes (~ 11.43 g) or a double dose of six prunes (~ 22.86 g) per day. Duration: 8 weeks.	II Exploratory	Liver function test showed significant reduction of serum alanine transaminase and serum alkaline phosphatase but no effect on serum aspartate transaminase and bilirubin
(Keßler *et al.*, 2002)	Germany	Plum juice (*P. domestica)*	Hypothesis: plum, cranberry- and blackcurrant juice may have an influence on the urinary composition and therefore on multiple risk factors of kidney stone formation. *n* = 12 healthy male subjects. Study design/methods: Participants control-fed a standardized diet daily with plum juice. Twenty four-hour urine sample collected. Sample size power: not stated Dose: 330 mL of plum juice. Duration: 5 days	II Exploratory	No significant effect on urinary biochemical or physiochemical parameters

*Clinical trials ranked using (NHMRC, 2000) Levels of Evidence Hierarchy where I is a systematic review (highest rating) and IV is a case series or cross-sectional study (lowest rating) and also classified as exploratory or confirmatory studies.

Table 9. Quality rating of included clinical studies using relevant criteria from the Delphi List, Cochrane Back Review Group and the CONSORT Statement (Verhagen *et al.*, 1998; Van Tulder *et al.*, 2003; Schulz *et al.*, 2010)

	J Nutr (2011) 106: 923–930	J Wom Health Gend-B (2002) 11: 61–68	Br J Nutr (2014) 112: 55–60	Appl Physiol Nutr Metab (2014) 39: 730–739	Am J Clin Nutr (2002) 76: 1422–1427.	J Am Coll Nutr (2007) 26: 170–181.	J Med Food (2005) 8(1): 41–46.	J Food Nutr Res (2011) 50: 229–236.
	n = 160 dried plum (*Prunus domestica*) 100 g/day versus dried apple Parallel 12 months	*n* = 58 dried plum (*P. domestica*) 100 g/day versus dried apple Parallel 3 months	*n* = 160 dried plum (*P. domestica*) 100 g/day versus dried apple Parallel 1 year	*n* = 23 dried plum (*P. domestica*) 90 g/day + resistance training versus resistance training case–control 6 months	*n* = 19 dried plum (*P. domestica*) 100 g/day versus habitual dietary simple sugars Cross-over 6 months	*n* = 6 dried plum/dried plum juice (*P. domestica*) 131 g versus selected fruits Cross-over 2 weeks	*n* = 10 plum juice (*P. salicina*) Single dose of 150 mL versus selected fruit juices Cross-over 18 days	*n* = 18 dried plum (*P. salicina*) 2 × 195 g/day Case series 5 days
A	Postmenopausal women (Osteopenic)	Postmenopausal women	Women with mild bone loss	Female breast cancer survivors	Postmenopausal women (Healthy)	Healthy volunteers	Healthy volunteers	Healthy volunteers
B	Yes	Yes	Yes	Yes	No	Yes	No	Not applicable
C	No (not feasible)	No (not feasible)	No (not feasible)	No (not feasible)	No (not feasible)	No	No	Not applicable
D	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
E	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
F	Yes	Yes	Yes	Yes	Do not know	Yes	Yes	Not applicable
G	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
H	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
I	Yes	Yes	Yes	Yes	Yes	Probably no	Probably no	Probably no
J	No	No	No	No	No	No	No	No
K	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
L	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
TS	10	10	10	9	8	9	8	7

	J Food Biochem (2012) 36: 159–170.	*Am J Clin Nutr* (1991) 53 (5): 1259–1265	*J Acad Nutr Diet* (2012) 112: 1158–1168.	*Curr Top Nutraceut R (2009)* 7: 157–160	*J Ayub Med Coll Abbottabad* (2010a) 22(1): 38–31	*J Funct Foods* (2015a) 12: 11–22	*J Funct Foods* (2015b) 14: 747–757	*Nutr Res* (2007) 27: 511–513.	*Internet J Nutr Wellness* (2009) 7: 1-1
	n = 2 plum juice (*Prunus. salicina*) Single dose of 400 mL versus 400 mL water Cross-over 1 week	*n* = 41 prunes (*P. domestica*) 100 g/day versus 360 mL grape juice Cross-over 8 weeks	*n* = 160 dried plum (*P. domestica*) 100 g/day versus dried apple Parallel 12 months	*n* = 8 prunes 143 g/day versus eight different fruits Cross-over	*n* = 259 prunes (*P. domestica*) 11.5 g or 23 g/day versus water Parallel 8 weeks	*n* = 21 plum juice (*P. salicina*) 200 mL/day versus prune juice/placebo Cross-over 28 days	*n* = 13 plum juice (*P. salicina*) 200 mL/day versus placebo Cross-over 28 days	*n* = 54 prune juice (*P. domestica*) 2 × 125mL/day Case-series 4 weeks	*n* = 36 Plum juice (*p. dometica*) 8 ounces/day vs psyllium and apple juice Cross-over 6 weeks
A	Healthy volunteers	Free living men with mild hypercholesterlemia	Postmenopausal women	Healthy young men	Pre-hypertensive patients	Healthy volunteers	Healthy volunteers	Adults with mild GIT symptoms	Adults with chronic constipation symptoms
B	No	Not stated	Not stated	No	Not stated	Yes	Yes	Not applicable	Yes
C	No (not feasible)	No (not feasible)	No (not feasible)	No (not feasible)	No (not feasible)	Yes	Yes	Not applicable	no (not feasible)
D	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

(Continues)

Table 9. (Continued)

E	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
F	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Not applicable	Yes
G	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
H	Probably no	Probably no	Yes	Yes	Yes	No	No	Yes	Yes
I	Yes	Yes	Yes	Yes	Yes	Yes	No	Probably no	Yes
J	No	No	No	No	No	No	No	No	No
K	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
L	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
TS	8	8	9	8	8	9	8	7	10

	Aliment Pharm Ther (2011) 33: 822–828	*Eat Behav* (2010) 11(3): 201–203	*Appetite* (2010) 3: 564–569	*J Am Diet Assoc* (2010) 9: 1322–1327	*J Appl Res* (2004) 4: 37–43	*Res J Pharm Biol Chem Sci* (2013) 2: 1195–1204	*J Pharm Sci* (2010b) 23: 463–466.
	n = 40 dried plum (*P. domestica)* 2 × 50 g/day versus psyllium Cross-over 14 weeks	*n* = 45 prunes (*P. domestica)* 40 g prune pre-load versus bread product Cross-over over 1 week	*n* = 19 dried plum (*P. domestica)* 238 kcal portion versus baked foods and water Cross-over	*n* = 26 Dried plum (*P. domestica)* 100 kcal portion versus low fat cookies Cross-over 4 weeks	*n* = 58 dried plum (*P. domestica)* 100 g/day versus dried apple Parallel 3 months	*n* = 170 dried plum and flixweed (*P. domestica)* 40–50 g/day Parallel 3 weeks	*n* = 107 prunes (*P. domestica)* three groups of either single dose, double dose or control case–control 8 weeks
A	Patients with chronic constipation	Normal weight individuals	Healthy female subjects	Healthy female subjects	Postmenopausal women	Iranian Hajj pilgrims	Healthy volunteers
B	yes	Yes	Yes	Yes	Yes	Yes	Yes
C	No (not feasible)	No (not feasible)	No (not feasible)	No (not feasible)	No (not feasible)	No (not feasible)	No (not feasible)
D	Yes	Yes	Yes	Yes	Yes	Yes	Yes
E	Yes	Yes	Yes	Yes	Yes	Yes	Yes
F	Yes	Yes	Yes	Yes	Yes	No	Yes
G	Yes	Yes	Yes	Yes	Yes	Yes	Yes
H	Yes	Yes	No	No	Yes	Yes	Yes
I	Probably no	Probably no	Yes	Yes	Yes	Yes	Yes
J	no	No	No	Yes	No	No	No
K	yes	Yes	Yes	Yes	Yes	Yes	Yes
L	yes	Yes	Yes	Yes	Yes	Yes	Yes
TS	9	9	8	9	9	8	10

An eligibility criteria specified, B randomization appropriate, C treatment allocation concealed, D similarity at baseline, E outcome measures and control intervention explicitly described, F co-intervention comparable, G outcome measures relevant, H adverse events and I drop-outs fully described, J sample size based on *a priori* power calculation, K point estimates and measures of variability presented for the primary outcome measure, L appropriate timing giving a total score (TS) of 12.

studied. This anabolic effect of dried plum supplementation has also been observed by others (Halloran *et al*., 2010) in animal models. Prevention of age-associated bone loss was evident because of this anabolic effect, while bone volume increased and already lost bone was restored.

Investigating further, Monsefi *et al*. (2013) observed the effect of plum extract on bone parameters in the offspring of pregnant mice as well as in non-pregnant mice. Plum extract was orally administered to the sample population, and results showed that in the non-pregnant mice, there was an increase in the femoral and tibial lengths and serum calcium content, while the foetuses and new-borns of the pregnant mice had higher osteogenesis index, which was calculated by dividing the ossified length by the total length of each bone.

Ovarian hormone deficiency, which is evident in postmenopausal women, is a known major risk factor for osteoporosis (Baron, 1993). For this reason, effect of plum consumption on bone health in human trials has been carried out mostly on postmenopausal women. A dietary supplementation trial compared the effects of consumption of dried plum (100 g) with dried apple (75 g) for 3 months on markers of bone turnover in postmenopausal women (Arjmandi *et al*., 2002). The difference in the amount of dried plum and dried apple compared was related to comparable quantities of energy, carbohydrates, fat and fibre, obtainable from 100 g of dried plum. Baseline and post-treatment values of serum and urinary biochemical markers of bone status showed that only dried plums significantly increased serum levels of insulin-like growth factor-1 and bone-specific alkaline phosphatase activity.

A similar longer-term randomized controlled study compared the effects of dried plum and dried apple on osteopenic postmenopausal women for 1 year (Hooshmand *et al*., 2011). In addition to similar results of Arjmandi *et al*. (2002), the authors observed that dried plum significantly increased bone mineral density of the ulna and spine.

In a slightly different study, Simonavice *et al*. (2014) examined the effects of resistance training and dried plum consumption on strength, body composition, blood markers of bone and inflammation in breast cancer survivors. They observed that even though the breast cancer survivors increased upper and lower body strength, no improvements were observed in their body composition and bone mineral density.

ANTIOXIDANT AND ANTIINFLAMMATORY ACTIVITY

The antioxidant property of plums has mostly been attributed to its high phenolic content (Ko *et al*., 2005; Lea *et al*., 2008). Research on this health effect has mostly been carried out with the ripe plum fruit or its products. Yu *et al*. (2009a) on the other hand studied the antioxidant effect of immature plum extract (IPE) on selected cancer cells *in vitro*. The authors observed that even though the IPE was effective in inhibiting growth of the cancer cells (human hepatocellular carcinoma HepG2 cells, Kato III gastric cancer cells, HeLa human cervical carcinoma cells, U937 leukaemia cells and MCF 7 hormone-dependent breast cancer cells), this inhibitory effect was not observed in the hormone-dependent breast cancer cells, and as the fruit ripened, there was a reduction in its inhibitory effect. In a similar study, Noratto *et al*. (2009) aimed to identify the phenolic fraction responsible for the potential chemopreventive and/or chemotherapeutic action in plum. They observed that all extract fractions were effective in exerting antioxidant effect on studied cancer cell lines with the flavonols and procyanidins more effective than the phenolic acids and anthocyanins. This result was also confirmed by Lea *et al*. (2008) who, in addition, observed that the synergic effect of the total phenolic content of the plum extract significantly increased its antioxidant activity.

Investigating this antioxidant effect on human colon cancer cells, Fujii *et al*. (2006) and Lea *et al*. (2008), in similar studies with prune and plum extract, respectively, observed that the extracts did not reduce the viable cell number of the human normal colon fibroblast cells while inducing apoptosis of cancer cells. Noratto *et al*. (2009), among other studies, also observed similar results in their study with breast cancer cell lines.

These results have also been confirmed in animal studies. Kim *et al*. (2008) observed that IPE inhibited the growth of hepatoma HepG2 cells and had a protective effect against benzo(α)pyrene induced liver toxicity by decreasing serum aminotransferase and hepatic contents of lipid peroxide. In addition to studying the antioxidant capabilities in animal studies, Mishra *et al*. (2012) also observed an anti-ulcer effect after feeding Wistar albino rats for 7 days with 100, 150 or 200 mg kg^{-1} of plum extract and inducing peptic ulcer by pyloric ligation. Gastric ulcerative index was estimated, which showed that the group pre-treated with plum extract had a significantly reduced gastric volume and a significantly lower ulcerative index. This anti-ulcer effect was also observed by (Cantu-Jungles *et al*., 2014) in which acute gastric ulcer was induced by administration of ethanol P.A. after different oral treatments, including prune polysaccharides, which showed a reduction and inhibition of the gastric lesion area. Yang and Gallaher (2005) further investigated the effect of plum on colon cancer risk factors whereby they observed that even though dietary supplementation with dried plum showed no inhibitory effect on aberrant crypt foci formation at the initiation stage of cancer and early progression, it was able to inhibit several risk factors associated with colon carcinogenesis. These include reduction in faecal total and secondary bile acid concentration, decrease in colonic β-glucuronidase and 7α-dehydroxylase activities and increased antioxidant activities.

Contrary to observing similar results with *in vitro* and animal studies, results from human trials have not been in agreement. A study that investigated the plasma antioxidant capacity changes after a meal observed that consumption of a meal containing dried plum or dried plum juice did not alter plasma antioxidant capacity (hydrophilic and lipophilic $ORAC_{FL}$) (Prior *et al*., 2007). This result was contradicted by the findings of Ko *et al*. (2005) that demonstrated that nine different fruit juices, including plum juice, exhibited significant antioxidant effects in human plasma within 30 mins of consumption by suppressing reactive oxygen species generation. Similarly, González-Flores *et al*. (2011) confirmed the

antioxidant capability of plums in young, middle-aged and elderly adults. After consumption of 195 g of plum twice a day for 5 days, there was a significant increase from baseline in urinary 6-sulfatoxymelatonin (an antioxidant) and total antioxidant capacity levels measured by colorimetric assay. Similarly, Netzel *et al.* (2012) observed that following consumption of the Queen Garnet plum juice, there was a threefold increase in hippuric acid excretion (a potential biomarker for total polyphenols intake and metabolite), an increase in urinary antioxidant capacity and a reduction in malondialdehyde excretion, which is a biomarker for oxidative stress.

COGNITIVE IMPROVEMENT

Cognitive improvement associated with consumption of plum has not been extensively studied in humans. Most of the available evidence is from animal studies. This effect on cognition has mainly been attributed to the antioxidant property of plums as a result its high polyphenolic content. In a study in which four groups of mice were fed a high-cholesterol diet, with either 2% or 5% plum powder supplementation, a significant difference was observed in the time taken to complete the Morris water maze task between the group fed just the high-cholesterol diet and the control group, as well as the 5% and 2% plum powder supplementation group (Kuo *et al*., 2015). In a similar study but slightly contradictory results, Shukitt-Hale *et al.* (2009) compared the effects of 100% plum juice and 2% dried plum powder supplementation to modify age-related deficits in cognitive function in aged rats. It was observed that there was an improvement in cognition with the plum juice, but not with the dried plum powder.

Using plum extract, Shahidi *et al.* (2013) supplemented the diets of three groups of mice with different doses (75, 100, 150 mg/kg). There was a statistically significant difference in the number of trials to acquisition in the passive avoidance test that evaluates learning and memory between the control group and the plum extract treated groups. The retention test also showed that the treated groups had increased step through latency in the retention in comparison with the control group. These results are in line with similar studies (Sharma and Sisodia, 2013; Kao-Ting *et al*., 2013) that demonstrate a beneficial health effect of plum on cognition.

Bouayed *et al.* (2007) examined the effect of chlorogenic acid from plums on anxiety-related behaviours in mice using the light/dark test, the elevated plus maze and the free exploratory test. Results showed a decrease in anxiety-related behaviours (anxiolytic-like effect) and protection of granulocytes from oxidative stress.

Plum consumption protected against oxidative stress induced by radiation with special attention to spatial learning. Sharma and Sisodia (2013) observed that plum possesses prophylactic ability against radiation-induced metabolic disorders and also improved spatial learning. Exposed mice that had received plum performed better by taking less time to reach the coloured platform in the circular water tank apparatus (proxy for spatial learning and memory). Similarly, Kao-Ting *et al.* (2013) studied the effect of plum consumption for 2 months on cognitive performance and expression of cerebral neurodegeneration-related protein in streptozotocin-induced diabetic rats. Cognitive performance, assessed using the Morris water maze, showed that the plum supplemented diet had a significant beneficial effect on spatial memory and learning. There was also a significant reduction in expression of cerebral beta-amyloid, which is evident in Alzheimer's disease. Significant decreases in hyperglycaemia, insulin resistance and oxidative stress in the sample of rats were also observed.

CARDIOVASCULAR DISEASE RISK FACTORS

Insulin resistance, a major risk factor for metabolic syndrome and selected cancers, presents a major public health concern (Tsugane and Inoue, 2010). Studying the beneficial health effects of plums on cardiovascular disease risk factors, Noratto *et al.* (2015) compared the effect of plum juice with peach juice and a placebo group, which received the same amount of sugar in either peach or plum juice in obese Zucker rats. Their results showed that the plum juice group had the lowest weight gain and also that plum polyphenols exerted the highest anti-adipogenic and antiinflammatory effects in fat tissues. This provides evidence of the reduction of mRNA levels of peroxisome proliferator-activated receptor associated with plum intake.

Negishi *et al.* (2007) studied the effect of prune extract on blood pressure elevation in stroke-prone spontaneously hypertensive rats for 5 weeks. They observed that prune extract supplementation in diet suppressed the elevation of systolic blood pressure but not diastolic blood pressure. A study by Gallaher and Gallaher (2009) on apoE-deficient mice, known to be susceptible to rapid development of atherosclerotic lesions when fed cholesterol, investigated the ability of dried plum supplementation to reduce atherosclerosis. The percentage arterial tree atherosclerotic lesion area was significantly lower in groups fed the dried plum supplemented diet (4.75%), either with or without cholesterol, compared with the group fed cholesterol without dried plum supplementation.

In human trials, results have been inconclusive. Chai *et al.* (2012) studied the effect of daily dried plum consumption in comparison with dried apple on cardiovascular disease risk factors in postmenopausal women over a 1-year period. Results showed that serum total cholesterol levels were significantly lower in the dried apple group in comparison with the dried plum group only at 6 months. There was also a cholesterol-lowering effect for serum total and low-density lipoprotein cholesterol at 12 months, but this was not significant. Neither dried apple nor dried plum had a significant effect on the serum levels of atherogenic cholesterol. Contrary to this observation, Tinker *et al.* (1991) observed that in adult men with mild hypercholesterolemia, supplementation with prunes significantly lowered plasma low-density lipoprotein cholesterol compared with a grape juice control group. A significantly lower faecal bile acid concentration of lithocholic acid was also reported.

Regarding the effect of prunes on high blood pressure, Ahmed *et al.* (2010a) conducted a study with three groups of pre-hypertensive patients who were randomized to receive on a daily basis, either a single dose of

prunes (11.5 g), a double dose (23 g) or a glass of water (control) for 8 weeks. Participants who received either the single dose or a glass of water on empty stomach in the morning showed significant reduction in both systolic and diastolic blood pressure, while the double dose was associated with only a reduction in systolic blood pressure. The control (water) group also had significant increase in serum high-density lipoprotein that was not seen by prune-treated groups

Plum juice supplementation with the novel-bred Queen Garnet plum that has higher anthocyanin concentrations than the usual variant (Santhakumar *et al*., 2015a) observed an inhibition of platelet aggregation induced by adenosine diphosphate, collagen and arachidonic acid.

LAXATIVE EFFECT

Studies have also been carried out on the commonly known laxative effect of prunes, which has been attributed to its high fibre content. Piirainen *et al.* (2007) studied the effect of prunes on individuals with mild gastrointestinal symptoms. This study observed that consumption of prune juice reduced the occurrence of difficulty in defecation. Similarly, consumption of a daily portion of plum juice before a meal in adults with chronic constipation softened the stool, provided immediate relief and participants showed more preference to prune juice than apple juice (Cheskin *et al*., 2009). Similar results were also observed with dried plum in patients with mild to moderate constipation by Attaluri *et al*. (2011) in which the effect was attributed to a synergistic effect provided by sorbitol, dietary fibre and polyphenols.

ANTI-ALLERGY AND ANTIMICROBIAL PROPERTY

On the anti-allergy capability of plum, Karasawa *et al*. (2012) carried out a study with prune extract diet supplementation and injection of mite allergen for 3 weeks. It was observed that with the prune extract supplementation, number of sneezing events, total and mite allergen-specific immunoglobulin E levels were significantly lower even though they were unable to identify any anti-allergic components in the prune extract.

Studying the antibacterial property of plums, Yaqeen *et al*. (2013) observed that when tested on five different gram-positive bacteria, ethanol extracts of prunes exhibited an antibacterial property. This antibacterial property was also observed by (Cevallos-Casals *et al*., 2006)

OTHER EFFECTS

Other reported beneficial health effects of plum include its effect on liver function in healthy individuals. In a clinical trial, Ahmed *et al*. (2010b) observed a significant reduction in serum alanine transaminase and serum alkaline phosphatase (clinical biomarkers of liver health) with no changes observed in serum aspartate transaminase and bilirubin.

Keßler *et al*. (2002) studied the effect of plum juice on urinary stone risk factors and observed that plum juice had no significant effect on urinary composition. However, a study that utilized the Australian Queen Garnet plum reported an increase in urinary antioxidant capacity (Netzel *et al*., 2012).

Farajian *et al*. (2010) studied the short-term effect of prunes included as snacks prior to a meal on energy intake and satiety in normal-weight individuals. This study demonstrated that a preload of prunes in comparison with a bread product before a meal resulted in lower energy intake at later meals, including lunch and the desert (910 Kcal ± 233 on prunes day vs 971 Kcal ± 249 on bread product day. *P* value 0.010) as well as increased satiety at all time points tested between the snack and meal. Similar studies have also observed similar results (Furchner-Evanson *et al*., 2010; Howarth *et al*., 2010)

DISCUSSION

This systematic literature review identified 73 peer-reviewed journal articles on the health effects of plum and its associated products. Despite an increase in plum-based research that has emerged over the past decade, the level of evidence remains low. Of 25 clinical studies, nine studies included randomization to a plum supplementation group, but only one of these studies adequately described the method of randomization and blinding. Nonetheless, results from some of the study outcomes are consistent. Considering bone health as the main study outcome, the polyphenols present in the plum appear to be responsible for the benefits. However, Hooshmand and Arjmandi (2009) suggested that even though dried plum polyphenols have some bone modulating properties, the synergistic effect of these polyphenols, together with potassium and vitamin K, is required to produce potent effects on bone mass and microarchitecture and to reverse ovariectomy-induced bone loss in mature animals. Regardless, compared with other dried fruits (apple, apricot, grape and mango), only the dried plum exhibited an anabolic effect on trabecular bone in the vertebra and prevented bone loss (Rendina *et al*., 2013).

Some of the findings from the *in vitro* studies have been confirmed in animal studies but remain to be confirmed in human clinical trials. Most of the available human trials used the dried version of plums rather than fresh fruit, thus limiting translation to dietary messages of the positioning of plums in a healthy diet. The drying process significantly decreases anthocyanin and flavonol content of plums (Piga *et al*., 2003). The effect of other processing methods on the antioxidant properties of plums has been studied by Valero *et al*. (2012). Blanching decreased the tannins and antiradical efficiency of the fruits but increased the total polyphenol content, while osmotic dehydration had no effect on the total polyphenol and ferric reducing power. Fresh plums also have a higher free radical scavenging capacity (superoxide and peroxy radicals) and antioxidant activity than dried plums (Morabbi Najafabad and Jamei, 2014). Regardless, prunes are known to contain higher levels of phenolic compounds than most fruits and also possess higher radical scavenging activity, even possibly

the highest in dried fruit and vegetable products present in human diet (Shahidi, 2012). Further studies are required to compare the health effects of fresh plum, plum juice and dried plum in human trials.

Extraction methodology is also an important factor in plum-based research as different solvents have shown some disparity in extracts. Estimating the antioxidant capacity of the whole plum fruit, Dhingra *et al.* (2014) observed that in extracting the bioactive compound in plum, the ethyl acetate and butanol fraction showed the most antioxidant potential in comparison with the hexane and aqueous fraction.

Evidence included in this systematic review was gathered from studies that differed in a number of ways, including population studied, study design, outcome measures and methods of randomization. This limits comparison between studies. Limitations related to different study designs are particularly evident in the animal studies that show inconsistent results. For example, Kuo *et al.* (2015) observed significant outcomes on cognition using the Morris water maze task on mice fed a high-cholesterol diet with 2% dried plum supplementation. Conversely, Shukitt-Hale *et al.* (2009) showed that plum juice, but not a dried plum powder (2% concentration), was effective in alleviating cognitive deficits in aged rats. This may possibly be explained by a difference in the dosage of nutrients provided in the two studies, or the food matrix, or both (Wesche-Ebeling *et al.*, 1996) but remains to be elucidated in dose-response studies.

There have been no reports on the side effects associated with daily consumption of plum and its associated products. Studies have shown that consumption of dried plum over a long period has no significant effect on the levels of insulin and glucose or bowel function (Hooshmand *et al.*, 2013; Lucas *et al.*, 2004). Regardless, plums are known to contain considerable levels of oxalates, which occur naturally and may increase the risk of kidney stone formation (Ruan *et al.*, 2013). High levels of oxalate in the body inhibit the absorption of calcium, thereby resulting in precipitation of calcium, which can result in stone formation in the kidney and bladder (Massey, 2003; Weaver *et al.*, 1987). Keßler *et al.* (2002) observed that plum consumption had no significant effect on the risk factors associated with kidney stone development. These potential side effects have not been reported with usual plum consumption; however, it is important to identify the upper level of safe intake.

The increased interest in plum-based research has been attributed to the fruit's high levels of polyphenols and more recently its anthocyanin (a sub-class of flavonoids) content. Anthocyanins are water-soluble plant pigments that are particularly conspicuous in fruits and flower tissues where they are responsible for the diverse range of red, blue and purple colours. Anthocyanins are one of the most versatile subclasses of flavonoids that are known to protect chloroplasts from photodegradation by absorbing high-energy quanta, while scavenging free radicals and reactive oxygen species. The key characteristic that differentiates anthocyanin glycosides from other subclasses of flavonoid glycosides is their ability to be absorbed after oral ingestion, although to a limited extent. In nature, about 17 different anthocyanins have been discovered, but only six (cyanidin, delphinidin, petunidin, peonidin, pelargonidin and malvidin) have been shown to be of dietary importance and are ubiquitously distributed (Jaganath and Crozier, 2010). The major anthocyanins found in the plum are cyanidin (3-rutinoside, 3-glucoside and 3-xyloside) and peonidin (3-rutinoside and 3-glucoside) (Usenik *et al.*, 2009). Anthocyanins are absorbed in the small intestine and colon and transported in human serum and urine, mainly as metabolites to reach target cells (Talavéra *et al.*, 2004; Kay, 2006). Anthocyanins are known to be natural antioxidants and have generated a great amount of interest among researchers in the last decade. This trend has also been observed among plum breeders as different varieties of plum are cultivated through hybridization. One of these hybrids is the Australian Queen Garnet plum, a hybrid of the Japanese plum developed through a breeding programme funded by the Queensland Government in Australia. This novel-bred Queen Garnet plum is known for its exceptionally high anthocyanin levels, reaching up to 277 mg per 100 g fruit (Fanning *et al.*, 2013). Even though levels of anthocyanin content in fruits progressively increase during fruit development and ripening, this is more than two times higher than the total anthocyanin content of regular plums that has been reported to range from 5 to 173 mg per 100 g across harvest years (Miletic *et al.*, 2012). The beneficial health effects of these levels of anthocyanin found in the Queen Garnet plum are currently being researched. Preliminary studies using this variant of plum have demonstrated antithrombotic activity in humans (Santhakumar *et al.*, 2015a) and a beneficial effect on metabolic syndrome in rat models, *in vivo* and *in vitro* bioactivity (Bhaswant *et al.*, 2015). It is important that similar studies be performed with different hybrids of plum to confirm their beneficial health effects in the fight against chronic diseases.

Other parts of the plum fruit that are usually discarded or used in animal feed may also provide food components that confer health benefits. The plum pomace, a by-product (pulpy residue) from plum juice has been reported to contain 38-49% dietary fibre and have antioxidant and anti-inflammatory properties that have been demonstrated *in vitro* (Milala *et al.,* 2013).

CONCLUSION

In conclusion, this systematic review has identified an emerging body of evidence that demonstrates the beneficial health effects of plum consumption. The largest amount of evidence to date relates to prevention and management of osteoporosis, which shows promising evidence as an adjunctive therapy. However, many of the study designs were of low quality; therefore, it is important that well designed human trials are conducted to confirm these observed effects. Consideration of the nutritional composition of plums and prunes and the effects of processing on their bioactivity is also important for future research. Elucidation of the mechanism of action of plum polyphenols, identification of potential adverse effects and the effects of dosage on outcomes is necessary to inform dietary guidelines for chronic disease prevention and management.

Conflict of Interest

The authors of this manuscript have no conflict of interest to declare.

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Appendix 1: Search Strategy: Medline (OVID)

	Searches
1	"plum*1".m_titl.
2	limit 1 to English language
3	Prunes.m_titl.
4	limit 3 to English language
5	"prunus domestica".m_titl.
6	limit 5 to English language
7	"prunus salicina".m_titl.
8	limit 7 to English language
9	2 or 4 or 6 or 8
10	(9 not "plum blossom needle").m_titl.
11	limit 10 to English language
12	(9 not "plum pox").m_titl.
13	limit 12 to English language
14	(12 not "plum curculio").m_titl.
15	limit 14 to English language
16	(15 not "plume").m_titl.
17	limit 16 to English language