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Dried Plums and Their Products: Composition and Health Effects–An Updated Review

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This paper describes composition of dried plums and their products (prune juice and dried plum powder) with special attention to possibly bioactive compounds. Dried plums contain significant amounts of sorbitol, quinic acid, chlorogenic acids, vitamin K1, boron, copper, and potassium. Synergistic action of these and other compounds, which are also present in dried plums in less conspicuous amounts, may have beneficial health effects when dried plums are regularly consumed. Snacking on dried plums may increase satiety and reduce the subsequent intake of food, helping to control obesity, diabetes, and related cardiovascular diseases. Despite their sweet taste, dried plums do not cause large postprandial rise in blood glucose and insulin. Direct effects in the gastrointestinal tract include prevention of constipation and possibly colon cancer. The characteristic phenolic compounds and their metabolites may also act as antibacterial agents in both gastrointestinal and urinary tracts. The indirect salutary effects on bone turnover are supported by numerous laboratory studies with animals and cell cultures. Further investigation of phenolic compounds in dried plums, particularly of high molecular weight polymers, their metabolism and biological actions, alone and in synergy with other dried plum constituents, is necessary to elucidate the observed health effects and to indicate other benefits.

Keywords Prunes, prune juice, sorbitol, chlorogenic acids, quinic acid, laxation

INTRODUCTION

Prunes are dried plums prepared from prune-making varieties of *Prunus domestica* L., such as French plums cv d'Agen, Italian prune plums cv Sugar, and cv President, and many European and Middle East plum cultivars. Unfortunately, there are instances in the literature where the authors refer to "prunes" when they mean fresh plums of unknown species and variety, probably because of the incorrect translation of the Latin name for the genus *Prunus* into English. It is often in case of the Japanese oriental plum (*Prunus salicina* Lindl.), the species which includes many varieties of plums grown now all over the world (popular varieties such as Red Beauty, Black Beauty, Santa Rosa, Queen Rosa, Cassleman, Black Amber, Angelino, Simka, Laroda, El Dorado, Friar, and Kelsey). However, Chinese, Japanese, and Korean authors also use terms "prune" or "plum" interchangeably for the *ume* plum (*Prunus mume*), which is genetically closer to apricots than to plums, and is sometimes called an Asian apricot. In China and Japan these fruits are often pickled or dried, but the final product is very different from the dried California plum. On the other hand, there are many plum varieties in Europe and Middle East that belong to the *Prunus domestica* L. species, which are not used for production of dried plums.

The purpose of this paper is to provide a critical review of recent studies (2000–2010) that link the consumption of dried plums/prunes and their products to health effects. The composition section of the report compiles the available data on dried plums and their products. The discussion of physiological effects includes also studies of fresh plums, sometimes not of prune-making varieties, and their products, because certain constituents are the same, albeit in different proportions. In every case the species' name and variety are clearly stated, if known, to avoid misunderstanding.

COMPOSITION OF DRIED PLUMS AND THEIR PRODUCTS

Carbohydrates

The previous review (Stacewicz-Sapuntzakis et al., 2001) organized then available data from various sources, among them food composition tables from the US Department of Agriculture

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Table 1 USDA and NDS-R composition tables

	Dried plums			Prune juice		
	SR 25	SR 25	NDS-R	SR 25	SR 25	NDS-R
Serving (g)[a]	100	42	47.5	100	256	256
Energy (kcal)	240	101	114	71	182	182
Total carbohydrate (g)	63.88		30.34			44.67
Available carbohydrate (g)		26.97			42.11	
Total sugars (g)	38.13	16.01	18.11	16.45	42.11	34.82
Glucose (g)	25.46		12.09			14.08
Fructose (g)	12.45		5.91			20.22
Sucrose (g)	0.15		0.07			0.51
Starch	5.11		2.43			
Total dietary fiber (g)	7.1	3.0	3.37	1	2.6	2.56
Insoluble fiber (g)			1.51			1.28
Soluble fiber (g)			1.87			1.28
Pectin (g)			1.09			
Sorbitol (g)	12[b]		5.70			15.38
Protein (g)	2.18	0.92	1.04	0.61	1.56	1.56
Fat (g)	0.38	0.16	0.18	0.03	0.08	0.08
Moisture (g)	30.92	12.99	14.69	81.24	207.97	207.97
Ca (mg)	43	18	20	12	31	31
K (mg)	732	307	348	276	707	707
Fe (mg)	0.93	0.39	0.44	1.18	3.02	3.02
Mg (mg)	41	17	19	14	36	36
P (mg)	69	29	33	25	64	64
Cu (mg)	0.281	0.118	0.13	0.068	0.174	0.17
Mn (mg)	0.299	0.126	0.14	0.151	0.387	0.39
Se (μg)	0.3	0.1	0.14	0.6	1.5	1.54
Zn (mg)	0.44	0.18	0.21	0.21	0.54	0.54
Vitamin A (μg RAE)	39	16	19		0	0
Beta-carotene (μg)	394	165	187	2	5	5
Alpha-carotene (μg)	57	24	27		0	0
Beta-cryptoxanthin (μg)	93	39	44		0	0
Lutein + zeaxanthin (μg)	148	62	70	40	102	102
Vitamin C (mg)	0.6	0.3	0.29	4.1	10.5	10.5
Vitamin E (mg a-tocopherol)	0.43	0.18	0.18	0.12	0.31	0.31
Vitamin K1 (μg)	59.5	25	28.26	3.4	8.7	8.7
Thiamin (B1) (mg)	0.051	0.021	0.02	0.016	0.041	0.04
Riboflavin (B2) (mg)	0.186	0.078	0.09	0.07	0.179	0.18
Niacin (mg)	1.882	0.79	0.89	0.785	2.01	2.01
Panthotenic acid (mg)	0.422	0.177	0.2	0.107	0.274	0.27
Vitamin B6 (mg)	0.205	0.086	0.1	0.218	0.558	0.56
Folate (μg)	4	2	2	0	0	0
Choline (mg)	10.1	4.2	4.8	2.7	6.9	7.17
Oxalic acid (mg)			4.37			8.7

Notes: [a]A standard serving of dried plums is 42 g, but 100 g were used in the majority of human trials.
[b]Sorbitol content is from USDA (1987) Sugar Content of Selected Foods.

(USDA) and European sources. During the last decade, USDA periodically updated their food composition data, improving reliability and including more nutrients. Table 1 provides the nutritional content of dried plums (100 g) and of prune juice (256 g, or 1 cup). These amounts probably represent the upper range of intake per day, since larger doses may not be feasible in intervention trials for adult subjects. The standard serving of dried plums is 40 g in food industry labeling, 42 g (five dried plums) in the USDA database, 47.5 g in the Nutrition Data System for Research (NDS-R, 2008; widely used by nutritionists to calculate dietary nutrient intake). All three sources consider one cup of prune juice (240 mL) to be a standard serving.

Available carbohydrates (sugars and starch) provide nearly all the energy from dried plums. In the latest USDA Standard Reference Release SR 2 (USDA, 2012) sugars are represented mostly by glucose and fructose (25.5 g and 12.5 g/100 g, respectively), with traces of sucrose and maltose. The total amount of sugars in SR 25 does not include sorbitol. Current SR 25 does not list sugar alcohols, but an older USDA publication (USDA, 1987) reported 12 g of sorbitol/100 g of dried plums.

The US Department of Agriculture does not provide data for the individual sugars in prune juice. The data from 1987 appear to be incorrect, because the proportion of glucose and fructose in prune juice is reversed (14.1 g glucose and 20.2 g fructose

Table 2 Carbohydrates in fresh prune-making plums, dried plums, and prune juice

Component (g/100 g FW)	Fresh prune plums	Prune juice	Dried plums
Total dietary fiber	2.7	1.1	9.1
Oligosaccharides	0.6	0.1	1.4
Glucose	15.0	4.9	20.6
Fructose	9.2	3.0	13.1
Sucrose	0.3	0.1	0.6
Sorbitol	5.8	2.8	9.1
Inositol	1.5	0.7	1.8

Adapted from Dikeman et al. (2004) and Bauer and Fahey (2004).

per 256 g, or 8 oz) compared with dried plums. However, these values are still used by the NDS-R program. The total amount of sugars in prune juice, reported in SR 25 (USDA, 2012), was not directly measured but calculated by difference after subtracting water, ash, lipid, protein, and total fiber content, and therefore it includes sorbitol. NDS-R uses the value of 15.6 g sorbitol per cup as the reported average content from the study of various kinds of prune juice (with pulp, no pulp, and reconstituted; van Gorsel et al., 1992; Stacewicz-Sapuntzakis et al., 2001).

An extensive study of carbohydrate composition examined 18 plum/prune products, and reported results on the basis of dry weight (DW) (Bauer and Fahey, 2004; Dikeman et al., 2004). The study included prune juice, dried plum powder, and three kinds of dried plums (pitted prunes, prune 52/26 with pits, and undersized prunes). Table 2 is adapted from this study, but the values are recalculated on the basis of fresh weight (FW, as consumed, edible portion) and the results for three kinds of dried plums are averaged. The data for glucose and fructose in dried plums are in good agreement with the USDA table, but the total content of sugars in prune juice is only half of that listed in SR 25 (USDA, 2010). The ratio of glucose to fructose in prune juice is the same as in dried plums. Although sorbitol was measured in the above-described study (Dikeman et al., 2004), the authors did not report it for individual prune products. However, the study report (Bauer and Fahey, 2004) provided sorbitol content of dried plums (average 9.1 g/100 g FW), and that of prune juice (7.1 g/cup). Very little oligosaccharides were found in dried plums (Table 2).

Dried plums have a relatively high content of inositol (1.8 g/100 g), while prune juice contains the same amount per cup (Table 2). In a survey of inositol content in common foods (Clements and Darnell, 1980), dried plums were reported to have 470-mg inositol/100 g and prune juice had 666 mg/cup, while fresh red and yellow plums contained insignificant amounts.

Dried plums contain 7.1 g of total dietary fiber per 100 g, while prune juice has 2.56 g per cup (256 g), according to USDA tables, which do not list separately soluble and insoluble fiber. A large serving of dried plums (100 g) delivers about 20% of the adequate intake (AI) of dietary fiber recommended for adults (25 g for women, 38 g for men; Institute of Medicine, 2005). Table 2 provides data for total dietary fiber from Dikeman et al.' (2004) study, which are slightly higher, 2.8 g/cup for prune juice and 9.1 g/100 g average for dried plums. This result is in good agreement with another study from France, which obtained an average of 9.2 g total dietary fiber per 100 g in dried plums, with 5.3 g of soluble and 3.9 g of insoluble fiber (Fatimi et al., 2007). The proportion of galacturonic acid (42%) in the soluble fiber indicated a predominance of pectins, and 26% of glucose in the insoluble fiber pointed toward cellulose as the main component. A review of nutritive values of fresh plums (Walkowiak-Tomczak, 2008a), which includes prune-making and other plum varieties, lists the following FW content ranges: 86–88% water, 0.8–1.0% pectin, and 1.3–2.4% total dietary fiber. Pectins were also measured in 12 varieties of *P. domestica* plums grown in one location in Czech Republic (Rop et al., 2009). The pectin content was very high, 2.2–3.5 g/100 g FW. The authors did not report moisture content of these plums. The average moisture content of prune-making plums from other studies is ∼80% (Somogyi, 2005). Stanley plums from Turkey contained 89% moisture (Ertekin et al., 2006), but fresh d'Agen plums from California in Dikeman et al.' (2004) study had only 57% water.

Minerals

Table 1 lists the updated values for minerals in dried plums and prune juice as reported in the SR 25 (USDA, 2012). Table 3 shows the proportion of the recommended dietary allowance (RDA) or adequate intake, which may be satisfied by a large serving of dried plums (100 g) or a cup of prune juice. The reference values in Table 3 are the highest-recommended values for adults, except for pregnant and lactating women, by the Food and Nutrition Board (Institute of Medicine, 1997, 1998, 2000, 2001, 2005). Dried plums (100 g serving) are a good source of copper (31% RDA), potassium (16% AI), manganese (13% AI), and magnesium (10% RDA). Prune juice (256 g) is similarly high in copper (19% RDA), manganese (17% AI), and potassium (15% AI), but also in iron (17% RDA). The relatively high content of iron in prune juice is difficult to reconcile with that of dried plums. Considering that the majority of the US population falls short on the nutrient needs for many minerals (97%, 70%, and 55% of population have inadequate intake of potassium, calcium, and magnesium, respectively; Nicklas et al., 2009), dried plums and their products may make a valuable contribution to meet nutritional recommendations. Although the dietary reference intakes have not been established for boron, the mean intake of boron in the US population is 1.15 mg/day and the highest intake from food is 3 mg/day (Institute of Medicine, 2001). A large serving of dried plums contains 2.2 mg of boron, while a cup of prune juice may deliver 0.6 mg of boron (Anderson et al., 1994).

The amount of minerals in dried plums and their products is directly related to the mineral content of fresh prune-making plums, which may be quite variable and depends on cultivar, soil, growing conditions, and agricultural practices (such as

Table 3 Percentage of dietary reference intakes (DRI) per serving

Nutrient	New DRI	% in dried plums	% in prune juice
Serving (g)		100	256
Available carbohydrate (g)	130	33.2	32.4
Total dietary fiber (g)	38	18.7	6.8
Ca (mg)	1300	3.3	2.4
K (mg)	4700	15.6	15.0
Fe (mg)	18	5.2	16.8
Mg (mg)	420	9.8	8.6
P (mg)	1250	5.5	5.1
Cu (mg)	0.9	31.2	19.3
Mn (mg)	2.3	13.0	16.8
Se (μg)	55	0.5	2.7
Zn (mg)	11	4.0	4.9
Vitamin A (RAE)	900	4.3	0.0
Vitamin C (mg)	90	0.7	11.7
Vitamin E (mg α-tocopherol)	15	2.9	2.1
Vitamin K1 (μg)	120	49.6	7.3
Thiamin (B1) (mg)	1.2	4.3	3.4
Riboflavin (B2) (mg)	1.3	14.3	13.8
Niacin (mg)	16	11.8	12.6
Pantothenic acid (mg)	5	8.4	5.5
Vitamin B6 (mg)	1.7	12.1	32.8
Foliate (μg)	400	1.0	0.0
Choline (mg)	550	1.8	1.3

Note: DRI – highest RDA or adequate intake (AI), except in pregnancy or lactation.

fertilizers). Table 4 shows the mineral content of fresh plums from various studies. USDA SR 25 values are for unspecified varieties of plums, and the range of values quoted in the Polish review (Walkowiak-Tomczak, 2008a) also includes unspecified varieties, possibly of *P. domestica* and *P. salicina*. Czech plum data (Rop et al., 2009) are for 12 local varieties of *P. domestica* (including prune-making plums). Stanley plums were grown in Turkey, where they are used for production of dried plums (Ertekin et al., 2006). Their content of calcium, copper, manganese, and zinc was much higher than the average values listed for the unspecified fresh plums in USDA SR 25.

Table 4 Mineral content of fresh plums from various studies (mg/100 g FW)

Mineral	USDA	Review, 2009	Czech plums	Stanley plums
Ca	4	6–45	7.1–11.4	13
K	104	120–208	160–398	127
Fe	0.11			2.3
Mg	5.0	4.0–8.0	6.4–11.6	2.5
P	11		20–37	9.6
Cu	0.038			1.5
Mn	0.034			0.3
Zn	0.07			1.2

Note: USDA data are from SR 25 (unspecified plum varieties).
Review, from Walkowiak-Tomczak (2008a), unspecified plum varieties.
Czech plum data are from Rop (2009), 12 varieties (*P. domestica)*.
Stanley plum data are adapted from Ertekin et al. (2006).

Vitamins

Vitamin values were also updated in the latest USDA SR 25 (Table 1). Table 3 indicates that dried plums are an excellent source of vitamin K1, phylloquinone, since 100 g serving covers 50% of the adequate intake. Dried plums also contain significant amounts of riboflavin (14% RDA), niacin (12% RDA), and vitamin B_6 (12% RDA) in a 100 g serving. A cup of prune juice (256 g) delivers similar amounts of riboflavin (14% RDA) and niacin (13% RDA), but also vitamin C (12% RDA) and, surprisingly, vitamin B_6 (33% RDA). Ascorbic acid is added to prune juice during processing, so different brands may contain varying amounts of vitamin C. One brand was reported to have as much as 61.4 mg ascorbic acid per cup, i.e., 68% RDA (Boato et al., 2002). Prune juice contains less fat-soluble vitamins than dried plums, because some pulp and skin are removed during processing.

The only vitamin mentioned prominently on the label of dried plums packaged in the United States. is vitamin A. According to new conversion factors recommended by the Food and Nutrition Board (Institute of Medicine, 2001), the provitamin A activity of carotenoids in plant food should be expressed in retinol activity equivalents (1 μg Retinol Activity Equivalent (RAE) = 12 μg β-carotene, or 24 μg other provitamin A carotenoids). The USDA SR 25 database for carotenoids in dried plums lists 394 μg β-carotene, 57 μg α-carotene, and 93 μg β-cryptoxanthin per 100 g (Table 1), which amounts to 39 μg RAE/100g. Therefore, 100 g of dried plums may deliver only 4.3% of vitamin A RDA, and a cup of prune juice has negligible vitamin A activity. The food industry still uses International Units (IU) of vitamin A activity (1 IU = 0.6 μg β-carotene, or 1.2 μg other provitamin A carotenoids), which should be applied only to pharmaceutics if at all. At the present time, the rules of conversion and calculation of vitamin A activity for food labeling purposes remain the same from 1993 (Federal Register). Calculated in IU, 40 g serving of dried plums has 313 IU, which is 6.3% of 5000 IU, the daily value (DV) for vitamin A (per 2000 kcal).

Dried plums have a high content of vitamin K1 (phylloquinone), higher than any other fruit, fresh or dried, and comparable to cashews and hazelnuts (Dismore et al., 2003). The range of vitamin K1 in US dried plums is 51–68 μg/100 g, while in fresh plums it is only 4.4–7.9 μg/100 g, which indicates that the analyzed fresh plums were probably not of a prune-making variety. High amounts of dietary vitamin K may interfere with anticoagulation therapy prescribed for thromboembolic disease patients, who must avoid certain foods, such as dark leafy greens (containing 300–880 μg vitamin K1/100g).

Organic Acids

Quantification of organic acids in dried plums has been a subject of controversy, since the older methods of analysis measured total acids and expressed them as equivalents of malic or

citric acid. Very careful repeated extractions with ion exclusion chromatography and electrochemical detection provided better data on organic acids in various fruits (Kayano et al., 2003a). Prune-making plums were found to contain 1.1 g of quinic acid and 0.29 g of malic acid per 100 g, while dried plums had 4.3 g and 1.1 g of these acids, respectively. Fresh Japanese plums (*Prunus salicina*) contained only 0.32 g quinic acid/100g, while it was not detectable in *ume* plums (*Prunus mume*). Prune juice may have lemon juice, lime juice, or citric acid (2.4 g/L), added as acidulants (Somogyi, 2005). The acids provide characteristic taste and tartness of dried plum. Possible health effects of quinic acid metabolites are discussed in the following sections.

Dried plums contain moderate amounts of oxalic acid (4.4 mg per 47.5 g serving), while prune juice has 8.7 mg per cup, according to NDS-R data (Table 1). It appears that the value for prune juice was calculated from the German data for "100% plum juice, *P. domestica*" (3.4 mg/100 mL). The same study (Honöw and Hesse, 2002) reported an average of 1.7 mg oxalate/100 g of fresh plums. An older assessment of oxalate in English diet found 3.4 mg/100 g in the stewed giant Victoria prunes (Zarembski and Hodgkinson, 1962). A low-oxalate diet, prescribed for people with calcium oxalate kidney stones, limits the consumption of moderate-oxalate foods to three servings per day, but high-oxalate foods (>7 mg/serving) should be avoided entirely (University of Pittsburgh Medical Center (UPMC), 2006).

Volatile Compounds

The flavor of dried plums depends to some extent on the volatile compounds, some of which are released in the mouth during chewing and may reach olfactory mucosa. A study of volatiles appearing during dehydration of prune-making plums found only 1-hexanol, nonanal, and an unidentified ketone in the headspace of whole fresh plums (Sabarez et al., 2000). The homogenization of fresh plums caused release of hexanal, 2-hexenal, and phenylacetylaldehyde. During simulated commercial drying (18 hours, 80°C, air velocity 5 m/s), periodic sampling of headspace revealed disappearance of the three C_6 compounds (hexanol, hexanal, and 2-hexenal) and the generation of benzaldehyde, ethyl cinnamate, and 2-furancarboxaldehyde after 7–9 hours. Benzaldehyde, with an almond-like odor, is a product of amygdalin degradation, while 2-furancarboxaldehyde is probably derived from Maillard reactions or caramelization of sugars.

The first step of the Maillard reactions involves formation of Amadori compounds, nonvolatile precursors of color, aroma, and flavor of processed foods. Dried plums were found to contain 2-furoylmethyl derivatives of lysine, γ-aminobutyric acid, alanine, and proline (20.6, 21.6. 4.5 and 3.6 mg/100 g, respectively), which are common Amadori compounds (Sanz et al., 2001).

Antioxidants

Antioxidant compounds in prune-making plums undergo considerable degradation during processing due to high temperature, cell disruption, and activation of oxidizing enzymes (Stacewicz-Sapuntzakis et al., 2001). The antioxidants remaining after processing are mainly phenolic compounds, but also include fat-soluble carotenoids and α-tocopherol, as well as water-soluble ascorbic acid.

Minor Antioxidants in Dried Plums

The best estimate of carotenoids in dried plums was the unpublished study by F. Khachik (2000, personal communication), which was used for carotenoid values in the USDA SR 25 data and for the calculation of vitamin A activity. The averages of 24 samples of dried plums, their standard deviation, and ranges for 13 carotenoids and isomers are listed in Table 5. All carotenoids measured in this study are absorbed in humans and appear in plasma after ingestion. Some of these carotenoids may be partially converted to vitamin A (all β-carotene isomers, γ-carotene, α-carotene, and β-cryptoxanthin). The concentration ranges for individual carotenoids are quite wide, depending on the original content in prune-making plums and degradation during processing.

Tocopherols and ascorbic acid are also greatly degraded in prunes and do not contribute much to total antioxidant activity. When two prune-making Croatian cultivars were processed into dried plums (Družić et al., 2007), their vitamin C content decreased from 8.6 and 9.8 mg/100 g to 2.5 and 2.6 mg/100 g FW, respectively. These results are in good agreement with earlier USDA estimates of vitamin C in dried plums (Stacewicz-Sapuntzakis et al., 2001), but the USDA SR 25 value for vitamin C in dried plums is only 0.6 mg/100 g (Table 1). The amount of vitamin C in dried plums depends on the variety of prune-making plums, drying parameters, and the duration of storage (Piga et al., 2003; Del Caro et al., 2004). Higher drying

Table 5 Carotenoids in dried plums (mean of 24 samples)

Carotenoid	μg/100g	SD	Range (min–max)
Lutein	107.7	43.7	58.0–223.1
Zeaxanthin	21.1	7.7	11.4–43.0
Anhydrolutein	5.3	1.7	3.1–10.8
α-Cryptoxanthin	5.8	2.2	2.8–11.4
β-Cryptoxanthin	44.5	20.9	14.5–91.6
Neurosporene	7.8	7.1	0.0–33.0
γ-Carotene	26.1	11.4	10.6–60.5
α-Carotene	22.1	13.2	10.4–68.5
trans-β-carotene	118.1	59.9	38.3–271.1
9-cis-β-carotene	34.4	17.8	13.1–83.5
13-cis-β-carotene	12.9	7.2	4.6–32.4
Phytofluene	10.0	5.7	2.0–25.0
Phytoene	16.0	7.5	4.4–34.8

Note: From Dr. Frederick Khachik, Department of Chemistry and Biochemistry, University of Maryland, College Park, MD (unpublished data, personal communication, December 1, 2009).

Table 6 Antioxidant capacity measurements for dried plums and prune juice

	Total ORAC (μmol TE/100 g)	H-ORAC (μmol TE/100 g)	L-ORAC (μmol TE/100 g)	TEAC (μmol TE/100 g)	TRAP (μmol TE/100 g)	FRAP (μmol Fe/100 g)
Dried plums:						
USDA, 2007	6552	6463	179			
Wu et al., 2004	8578	8399	179			
Prior et al., 2007	8244					
Prior et al., 2007	2127					
Pellegrini et al., 2006				1482	2300	6054
Prune juice:						
USDA, 2007	2036	2036				
Prior et al., 2007	2127					

temperature (85°C, followed by 70°C) destroyed more ascorbic acid than lower drying temperature (60°C) in two varieties of Italian prune-making plums, and a further ∼50% of vitamin C was lost during 4–12 months of storage (at 20°C, in polypropylene bags, relative humidity 50% inside the package).

Antioxidant Capacity Measurements

Total antioxidant capacity of foods is measured by various chemical assays, using different radical or oxidant sources. The oxygen radical absorbance capacity (ORAC) assay uses 2,2′-azobis(2-amidinopropane) dihydrochloride (AAPH) as a peroxyl radical generator, a fluorescein probe, and a Trolox (a water-soluble vitamin E analog) standard. Lipophilic (L-ORAC) and hydrophilic (H-ORAC) antioxidant capacities are measured separately on extracts of food, and the values added to provide total ORAC in Trolox equivalents (TE) (Wu et al., 2004). A similar assay using fluorescence of R-phycoerytrin is called total radical-reducing antioxidant power (TRAP). The Trolox equivalent antioxidant capacity (TEAC) is based on the ability of antioxidants to quench the 2,2-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical, compared to the Trolox standard. The method based on the reduction of ferric complex with 2,4,6-tripyridil-s-triazine (TPTZ) to ferrous form is named as the ferric reducing antioxidant power (FRAP) assay.

The values obtained by different assays on the same samples of dried plums (Pellegrini et al., 2006) are presented in Table 6, as well as the results from different studies conducted around the world. Table 7 shows that the antioxidant capacity per unit of FW is higher in dried plums than in prune-making plums, but not directly proportional to total phenolics content (Družić et al., 2007; Walkowiak-Tomczak, 2008b). Air drying preserved the antioxidant capacity of plums based on dry weight, and even increased it in plums dried at 60°C, while osmotic dehydration with subsequent air drying reduced it by 37–45% (Table 7, Walkowiak-Tomczak, 2008b). In an Italian study of two prune-making plum varieties, antioxidant capacity per unit of dry weight was measured using the radical 2,2-diphenyl-1-picrylhydrazyl (DPPH), and it increased significantly in both varieties of plums dried first at 85°C and then at 70°C (total time 38–44 hours; Piga et al., 2003). Continuous drying at 60°C (60–72 hours) increased antioxidant capacity in cv Sugar, but slightly decreased it in cv President.

The results of various chemical assays, based on different principles, cannot be compared directly and their biological relevance is debatable. The problem is whether the antioxidants in food can be absorbed and alter antioxidant status in vivo. Changes in plasma ORAC after consumption of dried plums or prune juice were measured in six healthy older women, who were given 315 mL prune juice, or 131 g of dried plums blended in 315 mL water, or 315 mL water (control) in a randomized

Table 7 Effect of processing on total phenolics and antioxidant capacity

	DW (%)	Total phenolics (mg CAE/100 g DW)	Total phenolics (mg CAE/100 g FW)	TEAC (μmol TE/100 g DW)	TEAC (μmol TE/100 g FW)
Fresh plums	15.9	1836	292	12220	1943
Dried plums:					
Air (60°C)	76.1	2140	1629	15,160	11,537
Air (40, 60, 80°C)	75.2	2448	3255	12,290	9242
Osmotic dehydration (24 hr, 60°C)	88.8	1347	1196	7730	6864
Osmotic dehydration (72 hr, 60°C)	88.4	1036	916	6670	5896
Adapted from Walkowiak-Tomczak (2008b)					
Fresh plums, var. Elena			174		
Fresh plums, var. Bistrica			231		
Dried plums, var. Elena			529		
Dried plums, var. Bistrica			562		
Adapted from Družić et al. (2007)					

Table 8 Total phenolics in dried plums and prune juice

	(mg GAE/100 g)	Range (mg GAE/100 g)	Catechin equivalents (mg/100 g)
Dried plums:			
USDA, 2007	745	165–1392	
Wu et al., 2004	1195		
Družić et al., 2007	529, 562		
Prior et al., 2007	1400		
Vinson et al., 2005			788
Karakaya et al., 2001			368
Prune juice:			
Boato et al., 2002	180.5		
Lugosi and Hovari, 2003			180.1
Prior et al., 2007	350		

crossover design (Prior et al., 2007). Although these doses of prune juice or dried plums had total ORAC values of 10.8 and 6.7 mmol TE, respectively, the plasma H-ORAC and L-ORAC of treated subjects did not differ significantly from controls during five hours post-dosing. However, in a study of 27 women (25–54 year old) consuming twice a day a snack of dried plums (100 kcal each) for two weeks, serum antioxidant capacity, measured by the TEAC assay, was significantly increased (Kaper et al., 2010). Equicaloric snacks of low-fat cookies had the opposite effect in these women.

Phenolic Compounds

Phenolic compounds are the main source of antioxidants in dried plums. Total phenolics (TP) for dried plums and prune juice measured in gallic acid equivalents (GAE; Wu et al., 2004) are reported in USDA tables of ORAC (USDA 2007b). The TP assay is based on the Folin–Ciocalteu colorimetric assay and calibrated against gallic acid, chlorogenic acid, or catechin solutions. Table 8 presents the results of TP determinations from various studies of dried plums and prune juice. Compared with other dried fruits, only dried cranberries and dates have higher values of total phenolics based on catechin equivalents (CE) (Vinson et al., 2005), but dried plums have the highest value among dried fruits when TP content is based on gallic acid equivalents (Wu et al., 2004; Pellegrini et al., 2006). However, the best standard for measuring total phenolics in dried plums and their products is probably chlorogenic acid, because the isomers of this compound are the main phenolics in prune-making plums and they are not greatly degraded during processing. The total phenolics in plums are nearly doubled when expressed on chlorogenic acid equivalents (CAE) instead of gallic acid equivalents (Chun and Kim, 2004). In a study of the effect of fresh plum processing on TP content of resulting dried plums (Walkowiak-Tomczak, 2008b), the value of total phenolics expressed in CAE/100 g dry weight increased in air-dried plums, but decreased in plums that were osmotically dehydrated in 70% sucrose and then air-dried at 60°C (Table 7). Calculated per unit of FW, total phenolics are always higher in dried plums than in precursor prune-making plums, due to the concentration effect (Družić et al., 2007; Walkowiak-Tomczak, 2008b), despite the degradation of phenolic compounds during heat processing.

Spiking of human plasma with food extracts, beverages, or antioxidant compounds may also provide an estimate of antioxidant activity, although it bypasses absorption and metabolism in the body. Prune juice was tested in vitro for the ability to inhibit human lipoprotein (LDL + VLDL) oxidation by 50% (IC_{50}) and increase lag time by 50% (CLT_{50}) (Vinson et al., 1999). Both parameters, expressed as μM concentrations of total phenolics, were similar for prune juice, coffee, and chlorogenic acid. Another study (Kasai et al., 2000) showed an inhibitory effect of various *high-performance liquid chromatography* (HPLC) fractions of "prune" extract on lipid peroxide-induced 8-hydroxydeoxyguanosine (8-OHdG) formation from deoxyguanosine in vitro. However, the extract was prepared from fresh plums of unspecified variety (personal communication from Dr. H. Kasai, October 6, 2010). The inhibitory fractions were determined to be isomers of chlorogenic acid. The authors also investigated the effect of chlorogenic acid on DNA oxidation in rat tongue. The animals treated with oxygen radical forming carcinogen, 4-nitroquinoline-1-oxide in the drinking water and fed with a diet containing chlorogenic acid (250 mg/kg) did not have an elevated level of 8-OHdG in DNA from tongue mucosa, compared with the treated rats fed with basal diet. Chlorogenic acid did not alter normal 8-OHdG formation in animals that were not treated with the carcinogen.

Isomers of chlorogenic acid (5-*O*-caffeoylquinic acid) are the principal phenolic compounds in dried plums, and also include neochlorogenic (3-*O*-caffeoylquinic acid) and cryptochlorogenic acid (4-*O*-caffeoylquinic acid) (Nakatani et al., 2000; Prior et al., 2007). Table 9 shows the proportion of these isomers in dried plums—the most abundant is neochlorogenic acid, cryptochlorogenic acid is fairly high, and chlorogenic acid is a minor component. In some studies cryptochlorogenic acid and chlorogenic acid were not separated by HPLC and reported together as chlorogenic acid (Piga et al., 2003). Many studies do not separate isomers and report only total chlorogenic acid (Amakura et al., 2000, for prune juice). Long drying of plums at low temperature (60–72 hours, 60°C,) partially degraded chlorogenic acids, while shorter drying at high temperature (38–44 hours, 85°C) preserved them in dried plums. Anthocyanins, mostly cyanidin-3 rutinoside, were totally destroyed by drying, and so were catechins (Piga et al., 2003). Small amounts of flavonoid rutin (quercetin-3-rutinoside) may persist in some varieties, which were exceptionally rich in this compound (cv President). The USDA database (USDA, 2007a) for the flavonoid content of selected foods lists quantities of flavonoids occasionally found in dried plums (Table 9).

The content of chlorogenic acids (94% of all extracted phenolic compounds) in dried plums accounts for only ~30% of their exceptionally high total antioxidant capacity, which suggests the presence of large amounts of other antioxidant molecules (Kayano et al., 2003b). Liquid chromatography–mass

Table 9 Individual phenolic compounds in dried plums and prune juice (mg/100 g)

	Prune juice, Amakura et al. (2000)	Prune juice, Prior et al. (2007)	Dried plums Nakatani et al. (2000)	Dried plums, Kayano et al. (2003b)	Dried plums, Prior et al. (2007)	Dried plums, USDA (2007b) Mean	Range
Chlorogenic acids (total)	19	101.6	107.7		152.5		
Neochlorogenic (3-CQA)		55.5	133		91.6		
Cryptochlorogenic (4-CQA)		38.1	31		51.1		
Chlorogenic acid (5-CQA)		8	6.7		9.9		
Gallic acid	2.1						
Caffeic acid			2.6				
Proanthocyanidins				62			
Cyanidin						0.71	0.0–2.4
Delphidinin						0.04	0.0–0.2
Quercetin						1.8	0.0–4.0

spectrometry (LC–MS) of dried plum extracts revealed the presence of 40 minor components (Table 10), mostly simple phenolic acids (caffeic, ferulic, gallic, protocatechuic, *p*-hydroxybenzoic, and *p*-coumaric), their glycosides and esters (Fang et al., 2002). However, they were not quantified and taken together would hardly explain the high ORAC value of dried plums. Japanese researchers extracted and characterized a plethora of minor novel compounds from California dried plums (Table 10), some of which had high ORAC value or acted synergistically with chlorogenic acids in vitro, raising their antioxidant capacity (Kayano et al., 2002, 2004a, 2004b; Kikuzaki et al., 2004). Again, the absence of quantification prevents concluding that some of them may be responsible for high antioxidant activity of dried plums.

Fresh plums (unspecified varieties) contain small amounts of catechin and epicatechin, but careful analytical techniques indicate high quantities of proanthocyanidins that are polymeric forms of flavan-3-ols. These are very difficult to extract from the plant matrix and do not fully elute from HPLC columns, or elute as a broad peak (Prior and Gu, 2005). The USDA database (USDA, 2004) lists the proanthocyanidin content for plums (unspecified varieties) with large proportion of high polymers (>10 units of catechin and epicatechin), but it does not contain values for dried plums. The USDA data are based on the survey performed by Gu et al. (2004), who did not find proanthocyanidins in dried prunes (unpublished observation). Fresh prune-making plums (cv d'Agen) were found to contain proanthocyanidins in the pulp (0.79 mg/g DW) and skin (0.59 mg/g DW) (Raynal et al., 1989). The authors suspected that these values may be underestimated due to the difficulty of assaying highly condensed polyphenols, which may be insoluble or bound to cell walls. Small amounts of proanthocyanidin dimers were also found in prune-making varieties of Polish plums (Węgierka Zwykła, Węgierka Łowicka, and Węgierka Dąbrowicka), but the sample preparation probably removed higher polymerization forms (Łoś et al., 2000). Japanese researchers found that large amounts of insoluble phenolic compounds are present in the residue remaining after ethanolic extraction of California dried plums

Table 10 Other phenolic compounds in dried plums

Fang et al. (2002)	Feruloquinic acids
	Coumarylquinic acids
	Trihydrocinnamoylquinic acids
	Dicaffeoylquinic acids
	Caffeoylshikimic acids
	Gallic acid and its hexoside
	Protocatechuic acid and its hexoside
	p-hydroxybenzoic acid and its hexoside
	Vanilic acid and its hexoside
	Methoxybenzoic acid and its hexoside
	Methoxybenzoic acid rhamnoside
	Caffeic acid and its hexoside
	Syringic acid and its hexoside
	Methoxycinnamic acid hexoside
	p-coumaric acid and its hexoside
	Ferulic acid and its hexoside
Kayano et al. (2002)	p-coumaric acid
	Protocatechuic acid
	Vanilic acid glucoside
	4-amino-4-carboxychroman-2-one
Kayano et al. (2003b)	(-)-epicatechin
	7-methoxycoumarin
Kayano (2004a, 2004b)	Coniferin
	Scopoletin
	Magnolioside
	Rutin
	Ferulic acid glucopyranoside
	Vanilic acid glucopyranoside
	(+)-Pinoresinol glucopyranoside
	9-glucopyranosyl-7-(4-hydroxy-3-methoxyphenyl-1-(3-hydroxy-propyl)-3-methoxy-dihydro-benzofuran
	Benzyl b-primeveroside
	2-(5-hydroxymethyl-2′,5′-dioxo-2′,3′,4′,5′-tetrahydro-1′H-1,3′-bipyrrole)carbaldehyde
Kikuzaki et al. (2004)	Abscisic acid
	Abscisic acid glucopyranoside
	Roseoside
	Dihydroxy-dimethyl-7-oxa-6-oxobicyclo-oct-8-yl-3-methyl-pentadienoic acid
	Dihydroxy-dimethyl-7-oxa-6-oxobicyclo-oct-8-yl-3-methyl-pentadienoic acid glucopyranoside
	Trihydroxy-dimethyl-7-oxa-6-oxobicyclo-oct-8-yl-3-methyl-pentadienoic acid

(Kayano et al., 2003b). These could be extracted after acid hydrolysis of the residue and the obtained fraction had high total phenolics and ORAC value. Colorimetric test for proanthocyanidins yielded 62 mg/100 g of dried plums. Subsequent research revealed the presence of oligomers (average polymerization = 5°) composed of catechin and epicatechin units, with the antioxidant potency higher than that of chlorogenic acid (Kimura et al., 2008).

Proanthocyanidins of dried plums should be further analyzed by phloroglucinolysis (Hagl et al., 2011), or thiolytic depolymerization (Nunes et al., 2008) that yield more accurate quantification. Such analysis of French and Portuguese fresh plums (not prune-making varieties) doubled the total amount of phenolics recovered from crude extract and revealed very high proportion of proanthocyanidins (45–92% of total phenolics, depending on plum variety).

Metabolites of Dried Plum Phenolics

The major phenolic compounds in dried plums, isomers of chlorogenic acid, are partially absorbed in the small intestine of humans, as inferred from studies with ileostomy subjects (Olthof et al., 2001). Seven healthy subjects without a colon ingested 1 g of chlorogenic acid or 0.5 g of caffeic acid. On the average, 67% of chlorogenic acid was recovered within 24 hours in ileostomy effluent, but only 5% of caffeic acid. Little chlorogenic acid was recovered from urine (0.3%), but 11% of caffeic acid dose was excreted. Caffeic acid was also excreted in urine after ingestion of chlorogenic acid (0.2% of the dose). It seems that 33% of the chlorogenic acid dose was absorbed unchanged in the upper gastrointestinal track, and extensively metabolized in the liver or kidney. Chlorogenic acid was not hydrolyzed in the stomach or the intestinal lumen of these patients. In subjects with healthy colons, chlorogenic acid is hydrolyzed into caffeic acid and quinic acid by the colonic microflora (Olthof et al., 2003). Human fecal bacteria were shown to metabolize both chlorogenic acid and caffeic acid in vitro (Gonthier et al., 2006). The major final product of bacterial and endogenous metabolism of caffeic and quinic acids is benzoic acid, subsequently conjugated with glycine by the liver or kidney, and excreted in urine as hippuric acid (Olthof et al., 2003).

There are many other minor metabolites appearing in plasma and urine in trace amounts, which could transiently exert antioxidant effects after ingestion of chlorogenic acid-rich foods (coffee, dried plums). Most of them are hydroxycinnamic acids (caffeic, ferulic) and their derivatives, of which the caffeic acid has the highest antioxidant activity (Shahidi and Chandrasekara, 2010). Very few studies describe the metabolism of dried plum phenolics in humans. Plasma and urine samples were collected from three healthy volunteers after ingestion of a single dose of 100 g California dried plums to check for the presence of hydroxycinnamates (Cremin et al., 2001). Chlorogenic acid was below the level of detection in plasma, but small amounts were recovered from urine, especially at two and four hours after dosing (19–35 nM concentration). Caffeic acid, in a free and conjugated forms (sulfate and glucuronate), was more abundant in urine (265–475 nM) and increased 1.5–3 fold after dried plum consumption. This study compared plasma levels of ferulic and caffeic acid before and two hours after ingestion of dried plums and found an increase of caffeic acid in two out of three subjects (~40 nM). Another study of 10 healthy volunteers followed plasma and urine levels of phenolic compounds for eight hours after ingestion of encapsulated green coffee extract as a single dose containing 170 mg (451 μM) chlorogenic acids (Farah et al., 2008). There was a great variability in the apparent bioavailability of chlorogenic acids among the subjects, from 8 to 72% of the dose, with a mean of 33%. The apparent bioavailability was calculated from area under the curve of plasma pharmacokinetic profiles, which were very different for individual subjects, with single or multiple peaks in plasma concentration. Maximal plasma concentration (C_{max}) of total chlorogenic acids was 14.8 $\pm$11.7 μM (~6 μg/mL), while the average time to reach it, T_{max}, was 3.1 $\pm$ 2.6 hours. Caffeic and ferulic acids were relatively minor phenolic compounds in plasma of these subjects, while caffeoylquinic and dicaffeoylquinic acids were predominant. A similar study of 11 healthy volunteers drinking one dose of instant coffee beverage containing 412 μM chlorogenic acids yielded very different results (Stalmach et al., 2009). The samples of plasma and urine were collected for 24 hours and the total recovery of metabolites in urine was similar in both studies (29% of the dose). Plasma C_{max} of total metabolites was only 1.15 $\pm$ 0.26 μM (<0.5 μg/mL) and there was much less individual variability among subjects. The differences between the results of these two similar studies of coffee phenolics metabolism may stem from the preparation of plasma and urine samples before chromatographic analysis (HPLC–photodiode array (PDA)–MS). The Farah et al. (2008) study treated the samples with β-glucuronidase and sulfatase, while the Stalmach et al. (2009) study did not. Although the second study found the metabolite forms of coffee chlorogenic acids in circulation, it may have had problems with recovery of all metabolites present in plasma. The major metabolites identified in plasma were dihydroferulic acid and its sulfate, ferulic acid sulfate, caffeic acid sulfate, and dihydrocaffeic acid sulfate (Stalmach et al., 2009). The major phenolic compounds excreted after green coffee extract consumption were sinapic, gallic, p-hydroxybenzoic, and dihydrocaffeic acid (Farah et al., 2008), while the other study identified dihydrocaffeic acid sulfate, feruloylglycine, dihydroferulic acid sulfate, and ferulic acid sulfate as the main urinary metabolites (Stalmach et al., 2009).

As early as 1914, it was noticed that consumption of dried plums (300 g) greatly increased the excretion of hippuric acid in the urine (Blatherwick, 1914; Blatherwick and Long, 1923) of two healthy subjects. Eating as little as 1.5 g of dried plums per kilogram body weight (BW) per day caused a striking elevation of hippuric acid in serum and urine in five healthy subjects (Cathcart-Rake et al., 1975). This effect was confirmed by a

Table 11 Composition of plum/prune products (per 100 g FW)

Component	Plum juice concentrate	Prune puree	Prune juice concentrate	Dried plum powder
Water (g)	29.6	30.0	30.5	3.5
Energy (kcal)	268	257	254	330
Protein (g)	2.28	2.10	2.34	3.00
Fat (g)	0.1	0.2	0.11	0.5
Total carbohydrate (g)	65.5	65.1	64.5	86.2
Total dietary fiber (g)	1.9	3.3	4.0	9.9
Soluble fiber (g)	1.7		3.7	5.0
Insoluble fiber (g)	0.2		0.3	4.9
Total sugars (g)		39		45
Glucose (g)	23.3	*22.3*	30.6	15.2
Fructose (g)	11.8	*13.9*	14.5	28.7
Sucrose (g)	3.7		0.68	1.1
Sorbitol (g)	17.0	14.1	17.8	25.1
Minerals				
Ca (mg)	45.3	31.3	41	72
Fe (mg)	1.03	2.80	1.52	3.00
K (mg)	834	852	752	1050
Na (mg)	65.3	23.0	52.2	5.0
Mg (mg)	51.5		45.8	
P (mg)	75.9	71.7	72.9	*108*
Zn (mg)	0.57		0.43	
B (mg)	1.98		2.60	*3.4*
Quinic acid (g)	3.38		3.22	
Malic acid (g)	0.86		0.85	
Vitamins				
Vitamin A (IU)	25.5	*2000*	119	1760
Vitamin C (mg)	Trace	4.3	2.83	*0.63*
Vitamin E (IU)	Trace		0.73	
Thiamin (mg)		0.04		
Niacin (mg)		2.5		
Panthotenic acid (mg)		0.43		
ORAC (μM TE)	13,040			*19,840*
Total phenolics (mg GAE)	987			*686*
Tannins (mg catechin equivalents)	19			
Gallic acid (mg)	312			
Chlorogenic acid (mg)	46.5			*4*
Neochlorogenic acid (mg)	198.5			*8.3*
Cryptochlorogenic acid (mg)				*10.8*
Rutin (mg)	0.07			

Note: The data are product specifications obtained from Sunsweet Growers Inc. (personal communication, June 15, 2010) except values marked in *italics* (prune puree: estimated glucose, fructose and vitamin A from USDA, 2012; dried plum powder: P and B from Hooshmand and Arjmandi, 2009; ORAC and total phenolics from Shukitt-Hale et al., 2009; chlorogenic acids from Yang and Gallaher, 2005).
ORAC values were converted to μM/100 g.

study of six subjects consuming prune juice (315 mL) or dried plums (131 g), whose urine was collected for six hours (Prior et al., 2002). Chlorogenic acid was not found in the urine of these six subjects, even after enzymatic hydrolysis with sulfatase and glucuronidase. Another major fraction of phenolics in dried plums, proanthocyanidins, cannot be absorbed in the intestine, but may be depolymerized in the colon by local bacteria and slowly converted to catechin and epicatechin monomers (Rios et al., 2003). The flavan-3-ol monomers are further metabolized to valerolactones, which may be absorbed and excreted in urine, or converted to benzoic, and finally hippuric acid (Olthof et al., 2003). Therefore, the increase in urinary excretion of hippuric acid within 48 hours after ingestion of dried plums or prune juice could reflect the metabolism and absorption of quinic acid and phenolic compounds in the alimentary tract.

Composition of other Commercial Products of Prune-Making Plums

Prune-making plums are processed into a variety of commercial products, which serve as ingredients in the production of other foods. Table 11 lists the components of fresh plum concentrate, prune juice concentrate, dried plum puree (prune puree), and dried plum powder according to industrial specifications except as noted. The various methods of processing prune-making plums result in specific differences in composition, although both concentrates and prune puree have similar water content (30%). Plum juice concentrate is made of fresh plum juice from mature plums cv d'Agen, and its composition is closest to fresh plums. It contains sucrose (3.7 g/100 g FW) and significant amounts of phenolic compounds, including gallic acid (rather

Table 12 Carbohydrates in plum/prune products (g/100 g FW)

	Plum juice concentrate	Prune puree	Prune juice concentrate	Dried plum powder[a]
Water	37.0	25.7	38.3	14.5
Total dietary fiber	1.0	5.2	4.2	10.8
Oligosaccharides	8.6	0.8	0.6	4.3
Glucose	20.2	16.7	21.2	22.8
Fructose	11.5	15.7	13.4	12.0
Sucrose	7.5	0.2	0.2	2.4
Sorbitol	10.7	12.6	10.2	11.5
Inositol	1.8	2.5	1.9	2.2

Note: [a]Dried plum powder, high moisture, 3% calcium stearate. Adapted from Bauer and Fahey (2004).

high amount, 312 mg/100 g FW). Prune juice concentrate is an extract of dried plums made by cooking dried plums to release soluble solids. The pulp is then removed from the extract and the juice is concentrated in high vacuum evaporator. The concentrate is used for production of prune juice. It contains very little sucrose (similar to dried plums) and insoluble fiber, which is removed with pulp. Dried plum puree is a blend of prune juice concentrate with dried plum paste, designed for use in baking to replace 50% of fat. The paste is made by cooking dried plums to 22–25% moisture, and blended with prune juice concentrate (25–30% paste, 70–75% juice concentrate).

Dried plum powder has been used in many laboratory animal experiments, as well as cell culture studies described in next sections. It is a commercial industrial food ingredient composed of 99% dried plums and 1% calcium stearate to prevent caking. Low-moisture powder contains up to 3.5% water, but one study reported as much as 14.5% moisture and 3% calcium stearate (Dikeman et al., 2004). Some composition data for dried plum powder in Table 11 are quoted from pertinent animal studies (Yang and Gallaher, 2005; Hooshmand and Arjmandi, 2009; Shukitt-Hale et al., 2009). Dried plum powder is 86% carbohydrates, including 10% of total dietary fiber. The industry-reported sugar composition, 28.7 g fructose and 15.2 g glucose/100g, is at odds with dried plums, which contain more glucose than fructose. There seems to be a relatively high amount of sorbitol, 25.1 g/100 g. However, a study of carbohydrate composition found 22.8 g glucose and 12 g of fructose/100 g of dried plum powder (Table 12), similar in proportion to dried plums (Bauer and Fahey, 2004; Dikeman et al., 2004). It also found 4.1% acid-hydrolyzed fat, no doubt due to the presence of calcium stearate, and 13.7% sugar alcohols (sorbitol and inositol). Calcium content of 72 mg/100 g in dried plum powder (Table 11) seems too low. Calcium stearate (at 1%) provides additional 66 mg of calcium in dried plum powder, or 198 mg calcium (as 3% calcium stearate) per 100 g.

The content of chlorogenic acids measured by HPLC is about seven-fold lower than in dried plums (based on dry weight), probably because production of dried plum powder involves further drying of prunes at high temperatures, which may degrade phenolic compounds (Gallaher and Gallaher, 2009). However, total phenolics measured by the Folin assay are in the range reported for dried plums.

HEALTH EFFECTS ASSOCIATED WITH MAJOR DRIED PLUM CONSTITUENTS

Gastrointestinal Health Effects

Dried plums have a long history of claims for preventing constipation as described in the previous review (Stacewicz-Sapuntzakis et al., 2001). In 1878, a preparation of "medicated prunes" was advertised to relieve constipation and "bilious disorders" (bloating, flatulence, heartburn, and dyspepsia; Kravetz, 2002). A similar preparation of prune concentrate and cascarin (Prucara) was described as very effective in constipated patients from several nursing homes (Stern, 1966). A laxative jam made of dates and dried plums was used to increase the frequency of bowel movements and decrease laxative medications in a group of hospitalized veterans (64–94 year old) in Canada (Durand et al., 1991). A geriatric hospital in Sweden introduced a mixture of buttermilk, bran, and dried plums for breakfast with excellent results (Lundberg, 1984). Prune whip yoghurt (yoghurt with pureed dried plums) was very effective in regulating bowel habits in a large group of elderly patients in a New York hospital (Ferrer and Boyd, 1955). A study of mildly constipated subjects in Finland compared control yoghurt (one cup/day) with test yoghurt containing galacto-oligosaccharides, linseed, and 12 g of dried plums in a crossover intervention (Sairanen et al., 2007). The subjects reported that the test yoghurt was more effective, but control yoghurt also increased defecation frequency from the baseline. The above-quoted studies used multiple agents to relieve constipation, so it is difficult to judge the effect of dried plums alone. However, in a systematic German population study, dried plums were perceived as the best food to soften stool by people suffering from constipation, irritable bowel syndrome with constipation, or healthy controls (Müller-Lissner et al., 2005). They were asked which foods or beverages altered stool consistency (open-ended question), and then were specifically questioned about prunes, bananas, coffee, tea, chocolate, beer, wine, and cigarettes.

The effect of dried plums or prune juice on intestinal motility depends on health and sensitivity of the subjects. In a study of 38 postmenopausal women, recruited for evaluating the effects of dried plum on bone biomarkers, who consumed 100 g dried plums or 75 g dried apples daily for three months, there were no differences in the self-reported bowel function between the

treatments (the amount of fiber was nearly equal) and no change from baseline before the treatments (Lucas et al., 2004). Snacking on dried plums (100 kcal) compared with low-fat cookies, twice a day for two weeks in a crossover design, promoted significantly softer stools in 29 younger women (25–54 year old) (Howarth et al., 2010). A study in Finland used specially prepared prune juice, made from plum concentrate, prune puree, water, and fructose to evaluate the effects on bowel function and gastrointestinal complaints (Piirainen et al., 2007). The 54 volunteers were followed for a week before treatment, two weeks of ingesting 125 mL prune juice twice a day, and one week after. There were fewer days with difficulty of defecation during the treatment than before, and the effect continued into the following week. However, more flatulence was reported during treatment.

Plum juice (PlumSmart), made from fresh prune-making plums with addition of prebiotic fiber (resistant dextrin), grape, carrot, and blueberry juices, was tested on 36 adult US volunteers with symptoms of constipation (Cheskin et al., 2009). The study lasted six weeks and involved drinking 6 oz of plum juice each day for two weeks, or 9 oz of apple juice with 3 g of psyllium fiber, or apple juice alone, in randomized order. The plum juice treatment resulted in softer stool than apple juice alone or with psyllium, and the relief of multiple constipation symptoms was as fast as with psyllium (within 24 hours). A similar study was conducted with dried plums (100 g/day) versus psyllium (12 g/day) in an eight-week randomized crossover trial (Attaluri et al., 2011). The subjects ($n = 40$) had symptoms of mild to moderate chronic functional constipation. Each treatment was administered in two doses per day (50 g dried plums or 11 g psyllium in a dose, each containing 3 g fiber), for three weeks. The number of bowel movements per week was significantly higher with dried plum treatment than with psyllium ((6.8 ± 0.5 vs 5.7 ± 0.6, $p = 0.002$), but both treatments improved constipation symptoms without causing any adverse effects.

The Chinese Institute of Nutrition and Food Safety (2005) conducted trials with dried plum extract on 120 subjects with mild constipation symptoms. The subjects were randomly divided into two groups: the intervention group received 50 mL of the extract per day for seven days, while the control group did not get any kind of treatment. The treated group had significantly increased defecation frequency, from 2.2 to 4.6 per week and decreased the score of defecation difficulty. The trial subjects did not exhibit any adverse reactions.

From the available evidence, it seems that dried plums and prune juice are considered as mild laxatives, but there is little information about possible diarrheal effect with increasing dose. There was a study comparing prune juice with sorbitol syrup (70%), castor oil, and sauerkraut juice for the purpose of developing a model of diarrheal illness of short duration and mild side effects (Reele and Chodos, 1985). When the volunteers ($n = 5$ or 6) ingested 4, 8, or 12 oz of prune juice, each dose caused only a single loose stool in one or two subjects, and no side effects were noted. A dose of sorbitol (30 mL, containing 21 g sorbitol) caused transient (two hours) diarrhea in all five subjects, and 60 mL (42 g sorbitol) resulted in a more severe, longer lasting diarrhea, accompanied by abdominal cramps. Two doses of sorbitol, each 45 mL (31.5 g), eight or six hours apart, produced similar response lasting 10 hours. Gastrointestinal effects of sorbitol are described in two reviews of tolerance of low-digestible carbohydrates (Livesey, 2001; Grabitske and Slavin, 2009). While small amounts of sorbitol have a humectant, stool-softening effect, large doses rapidly change fluid balance in the colon due to an osmotic effect. When the liquid stool is pushed behind hard stool by high-amplitude propagating contractions, the liquid portion exerts pressure on the bowel wall, like an inflating balloon, and may cause a severe cramping pain (McRorie et al., 2000). Solid sources are slower to cause diarrhea than liquids, divided doses are better tolerated, and an adaptation to slowly increasing doses may occur.

Sorbitol is generally recognized as safe (GRAS) by Food and Drug Administration (FDA), but processed food containing sorbitol requires a label warning about possible laxative effects if the consumption of sorbitol in this food is expected to exceed 50 g per day. European Codex Alimentarius requires such label for the dose of 20 g sugar alcohols per day. Such amount of sorbitol may be ingested in 167 g of dried plums ($\sim$20 prunes) or 328 mL (1.25 cup) of prune juice.

Intestinal motility may be aided by chlorogenic acids present in dried plums and prune juice. Increased peristaltic activity was observed in rats and mice after the application of chlorogenic acid (Chok and Lang, 1961), and similar effect is found in many human subjects after drinking coffee, which also contains this compound. Minor phenolic compounds of dried plums, caffeic, and ferulic acids were also shown to produce increased motility of gastrointestinal tract. Ferulic acid produced concentration-dependent contractions of isolated rat stomach fundus and guinea pig ileum, as well as increased gastric emptying rate and decreased intestinal transit time in the intact rats (Badary et al., 2006).

Dried plums may contain another substance that causes secretion of water and electrolytes into intestinal lumen, and also induces intestinal contractions. It is serotonin, a neurotransmitter and a regulator of gastrointestinal physiology. Fresh plums (unknown varieties) contain considerable amount of serotonin (3.6–5.7 μg/g; Feldman and Lee, 1985), and it would be advisable to check whether serotonin is also a constituent of dried plums. Exogenous serotonin was extensively studied in experimental animals (Salvador et al., 2000), and was found to increase intestinal fluid secretion and gut motility; however, it is unknown if the amount of serotonin in dried plum, if present, would cause similar effects.

Dried plums may also have a prebiotic effect, promoting growth of beneficial bacteria (saccharolytic anaerobes and aciduric organisms) in the colon. In vitro, sorbitol is fermented by colonic bacteria to short-chain organic acids, especially butyric acid, which in vivo maintains healthy colonic epithelium by contributing to an anti-inflammatory and anti-neoplastic environment (Livesey, 2003). Dried plums contain very little

oligosaccharides (Dikeman et al., 2004), but their high fiber and sorbitol content may provide additional fermentation substrate for healthful colonic bacteria. In rat, dietary sorbitol has a sparing effect on thiamine and other B vitamins (Morgan and Yudkin, 1957) due to a remarkable promotion of colonic bacterial synthesis. However, in an experiment with human subjects fed with sorbitol (70 g/day, 6–10 days) along with a low-thiamine diet, no significant increase of urinary excretion of thiamine was noticed, and the authors concluded that sorbitol did not increase colonic production of this vitamin (Peppler et al., 1960). Interestingly, not all of the 10 subjects in this experiment developed diarrhea despite the large dose of sorbitol.

Bone Preservation

Dried plums contain many compounds which could contribute to bone health and probably act synergistically. Among them, copper, boron, and vitamin K1 are particularly abundant and a regular intake of dried plums would help to satisfy the dietary requirements (Table 3). Vitamin K promotes bone mineralization, since it is a cofactor in γ-carboxylation of osteocalcin, which regulates the growth of hydroxyapatite crystals in the bone (Zittermann, 2001). Boron reduces urinary excretion of calcium and magnesium and elevates estradiol levels in postmenopausal women (Devirian and Volpe, 2003). Other minerals in dried plums, especially potassium, may also help to maintain bone mineral density (BMD).

Cell Culture Studies

Various polyphenols were also found to influence bone turnover. An extract was prepared from dried plum powder and used in a series of in vitro cell culture experiments. Mouse macrophage cells (RAW264.7) were used as osteoclast precursors to study the effect of dried plum phenolics on their differentiation and activity (Bu et al., 2008). The osteoclast differentiation was inhibited under normal, oxidative stress, and inflammatory conditions by incubation with the extracts, and the results were confirmed in mouse bone marrow cultures and resorption pit formation assay on dentin slices. Another type of cell, MC3T3-E1, mouse preosteoblastic cells, was used to evaluate the dried plum powder extract effect on osteoblast activity and mineralization (Kamkar et al., 2005; Kamkar et al. 2006; Hooshmand et al., 2008; Bu et al., 2009). Calcified nodule formation was dose-dependently increased with concentration of dried plum phenolics (0.5–1000 μg/mL; Kamkar et al., 2005; Bu et al., 2008). Alkaline phosphatase activity in cell medium was significantly increased by 100 μg/mL extract (Kamkar et al., 2006), and a similar effect was observed in the cells even at lower concentrations (2.5–20 μg/mL; Bu et al., 2009). IGF-I production was upregulated by a high dose of 1000 μg/mL in one laboratory experiment (Hooshmand et al., 2008) and by only 5 μg/mL in another (Bu et al., 2009). However, variability of response was so large that 10-μg/mL dose was not significantly different from control. Lysyl oxidase, an enzyme involved in bone matrix synthesis, was also upregulated by 5- and 10-μg/mL extracts, while the receptor activator of the NFκ-B ligand (RANKL) expression was downregulated under inflammatory conditions.

Judging from their effects on osteoblastogenesis and osteoclastogenesis, it would seem that dried plum phenolics may enhance bone formation and inhibit bone resorption, but there is a problem of these compounds reaching bone cells in vivo, since they may be poorly absorbed, quickly metabolized in the liver, or degraded by colon bacteria. However, the chlorogenic acids from green coffee extract (Farah et al., 2008) were found in the human plasma at $\sim$6 μg/mL, and the dose administered to study subjects was comparable to 100 g of dried plums or 170 mL of prune juice (Table 9; Prior et al., 2007).

Animal Studies

There is substantial research demonstrating that dried plum can not only prevent but also reverse hormone deficiency-induced bone loss in rodents, which has been recently reviewed and summarized (Hooshmand and Arjmandi, 2009). These animal studies added dried plum powder to a control diet at 5–25% (w/w) and quantified various parameters of bone metabolism and architecture after treatment. Ovariectomized female rats are considered a good model of accelerated bone loss occurring in postmenopausal women due to an increased rate of bone turnover and decreased intestinal absorption of calcium. When the treatment was started immediately after ovariectomy, the high dose of 25% dried plum powder in the diet prevented the decrease of bone mineral density of lumbar vertebra and femur (Arjmandi et al., 2001). These results were recently confirmed in similar experiment with ovariectomized mice (Rendina et al., 2009) receiving dried plum powder diets after the operation.

Another study examined the therapeutic effect of dried plum feeding on pre-existing bone loss. Ovariectomized rats were allowed to lose bone for 40 days on a control diet before 60-day treatment with dried plum powder (Deyhim et al., 2005). Bone mineral density of femur and tibia was restored at the low dose of 5% dried plum powder, while that of lumbar vertebra improved on 25% dose. The structural and biomechanical properties were also improved, compared with ovariectomized controls. A similar study included a positive control group injected with parathyroid hormone (PTH; Lim et al., 2009). It was found that dried plum powder partially restored bone density, strength, and structure, and decreased serum levels of precollagen I N-terminal propeptide, a marker of bone turnover, while PTH had no effect on PINP.

Bone loss may also occur due to inactivity (skeletal unloading) in immobilized patients or in astronauts at zero gravity. Such a study was conducted on rats, which were hindlimb unloaded for 21 days to induce osteopenia (Smith et al., 2003). It was followed by 90 days of ambulation with PTH injections or dried plum powder diet. The bone recovery during re-ambulation period was similar on both treatments, resulting in comparable bone mineral density, bone strength, and bone structure.

Older men also experience osteoporosis, albeit at a slower rate than postmenopausal women. Castrated rats provide a model of male osteoporosis and were therefore investigated using dried plum powder-supplemented diet (5%, 15%, and 25%; Franklin et al., 2006). After 90 days treatment, dual energy x-ray absorptiometry (DXA) scans indicated that bone mineral density loss of whole skeleton was prevented by the medium and high doses of dried plum powder. The low dose was effective for bone mineral density of lumbar vertebra and femur. In another study, the male rats were castrated and allowed to lose bone for 90 days before the start of dried plum powder diet (25%) or PTH injections (Bu et al., 2007). The observed reversal of bone mineral density loss in the whole skeleton and individual bones was comparable on PTH regime and dried plum powder diet, and was accompanied by favorable changes in bone structure.

Interesting results were obtained with the mouse model of age-related bone loss (Halloran et al., 2010). Adult (six months) and old (18 months) male mice were fed with normal diets or isocaloric diets containing dried plum powder (15% or 25%, w/w). After six months on the 25% dried plum diet, the bone volume increased by 50% in adult and by 40% in the old mice, while those on control diet lost 24% and 28% bone, respectively. Thus, dietary plum not only prevented loss but also replaced bone already lost due to aging. The effects were larger in adult rather than in old animals. The lower dose of dried plum was not effective in the old mice and their response to the higher dose was similar to the response of adult mice on the lower dose. The effects of dried plum reached a steady state after three months and further supplementation maintained gain in bone mass. However, the indices of bone formation, resorption, and bone mineral density did not vary significantly on different diets.

In order to understand the mechanism of bone-sparing action of dried plums, various physiological processes, hormones, and enzymes involved in bone metabolism were studied. When rats are injected with tritiated tetracycline, it is deposited in bones and released when bone is resorbed. Subsequent urinary excretion of tritium is a measure of bone resorption. This test was used to investigate the effect of various food items on bone turnover in young male rats (Muhlbauer et al., 2003), among them also "prunes" (7.7% in diet). However, the "prune" powder used in this survey was a freeze-dried powder made of fresh plums of unknown variety. It may have had quite different composition from dried plum powder used in the previously described series of experiments. After 10 days of feeding, plum powder significantly decreased this marker of bone resorption. Similar results were obtained with dried plum powder in castrated male rats, using urinary excretion of deoxypyridoline (Dpd), a collagen degradation product, as a measure of bone resorption (Franklin et al., 2006). Castrated rats exhibited significantly higher excretion of Dpd, but the dried plum powder (5%) diet reduced it to normal levels found in intact animals, and higher doses were even more effective (57% reduction at 25% dose, compared to control diet). Two bone proteins involved in osteoclastogenesis (bone resorption), osteoprotegin, and receptor activator of NFκ-B ligand were upregulated in castrated rats, but dried plum powder treatments decreased their expression in the bone in a dose-dependent manner. Besides decreasing bone resorption, dried plum powder diets may also stimulate bone formation through insulin-like growth factor (IGF-I) elevation observed in both male and female rats. However, serum IGF-I levels were significantly increased just by the removal of gonads in both sexes of rats, and the lowest levels were observed in normal controls on standard diets. IGF-I is supposed to decrease immediately after menopause in women, and to correlate with bone mass in aging people.

Recently, it was found that freeze-dried blueberry powder (10% in diet) promoted bone growth in young male and female rats, which started the ad libitum diet at 20 days of age and continued it for 14 or 40 days (Chen et al., 2010). Blueberries contain various phenolic compounds, among them chlorogenic acid, which was not quantified in the blueberry powder in this study. However, there was 6–10-fold increase in concentration of seven phenolic acids in the serum of blueberry-fed rats, the most prominent being hippuric acid (from 0.5 to 3.3 nM/L). Both serum of blueberry-fed rats and an artificial mixture of the seven phenolic acids (at the same concentrations as in the serum) were able to stimulate osteoblastic cell differentiation in vitro.

Human Studies

When dried plums (100 g) were consumed by postmenopausal women (n = 18) for 90 days, the serum levels of IGF-I increased significantly, and so did total alkaline phosphatase (AP) and bone-specific alkaline phosphatase (BSAP) activity, all markers of bone formation (Arjmandi et al., 2002). The control group (n = 20) consumed equicaloric amount of dried apples (75 g) and also experienced a significant increase in serum AP. The increase in BSAP activity was not significant on the dried apple supplement, but the final values after both treatments were identical. It is possible that dried apples also exert some beneficial effects, and a crossover trial with the same group of women could have produced more decisive results, especially with a control period without any dried fruit supplement. A three-month study is a short time for human bone mineral changes, so another trial, involving 100 postmenopausal women, receiving dried plum (55 subjects) or dried apple (45 subjects) supplements for a whole year, was conducted by the same group (Arjmandi et al., 2007; Hooshmand et al., 2011). In addition to biochemical markers in blood samples collected at 0, 3, 6, and 12 months, DXA measurements of bone mineral density and bone mineral content were performed at baseline and end of the study. The consumption of dried plums preserved bone mineral density of ulna and spine significantly better than the consumption of dried apple. The effect may be partially due to suppressing the rate of bone turnover, as a significant decrease was observed in serum tartrate resistant acid phosphatase after three months (and maintained thereafter), and in serum BSAP after 12 months on dried plum treatment. The dried apple treatment did not produce consistent changes in biomarkers except an increase in serum osteocalcin.

Calcium Absorption and Bone Health

There may be another mechanism involved in the bone response to dried plum feeding. Many sugars were found to enhance calcium absorption in the ligated ileum segments of anesthetized rats (Vaughan and Filer, 1960). A test solution of labeled calcium, ^{45}Ca, and 50 mg of various sugars were injected into the ligated segments, and the rat femurs were removed after four hours and checked for radioactivity. Sorbitol increased the absorption of calcium into the bone by 210%, glucose by 156%, and fructose by 233%. The authors did not find this enhancing effect of sugars in the duodenum, where glucose and fructose are absorbed. Sorbitol is poorly absorbed in the duodenum, passes to the ileum, and improves calcium absorption in the lower regions of the intestinal tract. Another experiment involved feeding rats for eight weeks on diets containing 20% sorbitol (Knuuttila et al., 1989). Although no diarrhea was observed, sorbitol-fed rats gain significantly less weight, excreted more calcium in urine, and retained more calcium in bone. Their serum calcium level also increased significantly. Bone resorption on the sorbitol-supplemented diet was also studied using rats that were pre-labeled with tritiated tetracycline (Mattila et al., 1996). Sorbitol, 1 mol/kg, i.e., 18.2%, was added to a basal diet. The rats were maintained on experimental diets for one month and experienced continuous diarrhea, which decreased their weight gain despite a normal rate of food intake. The excretion of tritium in urine was reduced after one day on the sorbitol diet and the effect was maintained during the whole experiment. Radioactivity retained in scapula was significantly greater on the sorbitol diet, but in the tibia the increase did not reach statistical significance. These results indicate that sorbitol supplementation may increase calcium absorption from the intestine and suppress bone resorption. This effect could have been partially responsible for the effects of dried plum powder diet in previously described animal experiments, since the diets contained from 1 to 6% sorbitol (calculated from sorbitol content of dried plum powder).

There are some indications that chlorogenic acid and caffeic acid may stimulate the production of hydrochloric acid in the stomach of healthy volunteers (Chok and Lang, 1961), who drank 250 mg of either of these compounds in 200 mL of water. Quinic acid was not effective in this test. Both regular and decaffeinated coffee stimulates gastric acid secretion (Cohen and Booth, 1975; Viani, 1988), probably due to similar content of chlorogenic acid. It is therefore possible that chlorogenic acids from dried plums may improve the absorption of calcium from food and supplements, especially in older persons with impaired gastric acid production.

Antimicrobial Effects

Dried and fresh plum products have been tested for the ability to suppress the growth of food-borne pathogens in liquid broth and ground meat (Fung and Thompson, 2001; Fung and Thompson, 2009). There was a significant suppression of *Salmonella typhimurium*, *Escherichia coli* O157:H7, *Listeria monocytogenes*, *Yersinia enterocolitica*, and *Staphylococcus aureus* in liquid medium and uncooked meat (ground beef, pork sausage) at a 3–6% concentration of dried plum puree and fresh plum juice concentrate.

Dried plums may also exert antibacterial action within the alimentary and urinary tract because of their unique constituents. Sorbitol, which is used in control of dental caries as an ingredient of chewing gum, has low cariogenicity compared to sucrose and glucose (Burt, 2006), which are abundant in other dried fruits and candy. Dental plaque bacteria do not metabolize sugar alcohols, so chewing dried plums instead of other sweets may suppress cariogenic flora. The acids produced by the dental plaque bacteria demineralize enamel surfaces and may lead to formation of caries. Phenolic compounds of dried plums may also interfere with microbial pathogens in the mouth. The proanthocyanidin fraction of cranberry juice was found to suppress in vitro the proteolytic action of bacteria responsible for chronic periodontitis (Bodet et al., 2006). The proteinases of these bacteria degrade gum and bone tissue in periodontal pockets.

Interaction of phenolic compounds and nitrite in stomach may produce nitric oxide, as was found in volunteers after eating lettuce (source of nitrate) and different polyphenol-rich foods (apples, berries, onion, cherries, tea, and red wine; Rocha et al., 2009). Considerable amount of nitric oxide was found in air regurgitated from the stomach during the 30-minute period after eating these foods. The reaction was confirmed in vitro with simulated gastric juice, nitrite, and various phenolic compounds (chlorogenic acid, procyanidin dimers, catechin, epicatechin, quercetin, and epicatechin-3-*O*-gallate). Nitric oxide may induce gastric smooth muscle relaxation and kill *Helicobacter pylori*. In addition, the adhesion of *H. pylori* bacteria to stomach walls may be inhibited by proanthocyanidin polymers (Burger et al., 2002) as found in vitro with high molecular weight component of cranberry juice. It prevented some strains of these bacteria from binding to human gastric mucus and to a monolayer of human gastric epithelial cells in dose-dependent way. *H. pylori* infection is associated with stomach ulcers and is a risk factor for gastric cancer.

Cranberries seem effective in the prevention of urinary tract infections (UTI), especially in women, and the original hypothesis of their mode of action centered on acidification of urine (Kinney and Blount, 1979). However, cranberries and their products do not have a reliable acidifying effect (pH 5 and below) required for bacteriostatic action (Bodel et al., 1959). Nevertheless, both cranberry juice and urine of mice or humans ingesting cranberry products were found to inhibit the growth of bacterial cultures (mostly *E. coli*, the main culprit in UTI; Sobota, 1984). Fractionation of cranberry extract indicated that the active components of cranberries were fructose and proanthocyanidins, which reduced adherence of bacteria to uroepithelial cells (Howell, 2007). Both proanthocyanidins and fructose are present in dried plums and prune juice, but there are no studies of possible effects of dried plums on UTI prevention. However, fructose or proanthocyanidins are not found in any significant amount in urine after cranberry ingestion, but the metabolites of

proanthocyanidins or other cranberry constituents may be present in sufficiently high concentration to prevent bacteria from adhering to urinary epithelium and/or inhibit their growth. One of these metabolites is hippuric acid, produced from proanthocyanidins, chlorogenic acids, and quinic acid, all these compounds being present in prunes and their products. Prune-making plums contain more quinic acid than cranberries (1.2 vs 0.88 g/100 g), and dried plums have as much as 3.7–4.3 g/100 g (Kayano et al., 2003a). Consumption of dried plums (300 g) increased the excretion of hippuric acid in the urine (Blatherwick and Long, 1923) of a healthy young female subject by 8 g/24 hours. The subject was also tested with an equal weight (300 g) of cranberries, which produced less than half the amount of hippuric acid excretion from dried plums. Similar results were found for a male subject in the same study. There was an increase in acidity of urine amounting to 0.5 unit of pH in the male and 1.0 unit in the female. In another study, 1.5 g of dried plums per kilogram body weight per day elevated hippuric acid in serum and urine of five healthy subjects (Cathcart-Rake et al., 1975). On an average, ∼100 g of dried plums increased hippuric acid excretion by 2.6 g/24 hours, which is in perfect agreement with the earlier study. In a shorter study, six older women consuming a single dose of prune juice (315 mL) or dried plums (131 g) excreted on average 0.77 g or 0.24 g of hippuric acid, respectively, within six hours (Prior et al., 2002).

Although it has not been established that excretion of hippuric acid is responsible for the antibacterial effect of cranberries in the urinary tract, the drug methenamine hippurate (Hiprex) is still used to prevent recurrent UTI. The hippuric acid moiety was originally introduced to increase the activity of methenamine, and the directions still advise eating cranberry and prune products during treatment (RxList, 2013).

Modulation of Immune Response

Certain foods or their constituents may promote wound healing, alleviate symptoms of autoimmune diseases, or increase resistance to infection (Hughes et al., 2004). Very little is known about the effect of dried plums on immune response in vivo. The addition of prune whip yoghurt (one cup) to the diet was very effective in healing a persistent varicose ulcer on the leg of a diabetic woman, and dermatitis, rash, and itching in other patients, especially rectal pruritus (Ferrer and Boyd, 1955). However, the effect may have been partial or whole due to yoghurt, which contained beneficial probiotic bacteria. When chickens were raised on a standard diet supplemented with freeze-dried powder of oriental plum (*P. salicina*) at 1% dose, and infected with coccidosis parasite, they grew better than on the control diet and shed less oocysts in their feces (Lee et al., 2008). Their spleen lymphocyte proliferation was increased even at the 0.5% dose, and intestinal lymphocytes had an increased expression of mRNA for interferon-γ and interleukin-15 at 1% dose of plum powder. These results indicate that oriental plum may enhance immune response in poultry against protozoan infection. However, the mouse splenocytes proliferation was not enhanced by a similar freeze-dried powder of oriental plum added to an in vitro culture (10–500 μg/mL; Lin and Tang, 2007).

On the other hand, there is a need for dietary means to induce immunosuppression after organ and bone marrow transplantation (Hushmendy et al., 2009) and in over 80 recognized autoimmune diseases. Dried plum powder extracts were tested in vitro on mouse splenocytes stimulated with concavalin A, and decreased their production of tumor necrosis factor (TNF-α), but not of interleukin-6 (Rendina et al., 2009). The extracts also reduced the production of nitric oxide and cyclooxygenase-2 in mouse macrophage line RAW264.7 cells, stimulated with bacterial liposaccharide, i.e., endotoxin (Kumar et al., 2009). These results suggest that there may be immunomodulatory properties to dried plums; however, significantly more research needs to be done to understand this relationship.

Recent experiments have demonstrated that dietary soluble fiber (pectin) may have profound effects on the immunologic response to endotoxin from *E. coli* O127:B8 strain (Sherry et al., 2010). When mice were fed with diet containing 10% pectin for at least five weeks, and then injected intraperitoneally with the endotoxin, they became less sick and recovered faster than mice fed with insoluble fiber (5% or 10% cellulose in diet). Interleukin-4 production was significantly increased in many tissues, especially in the gastrointestinal tract, of pectin-fed mice, and the isolated macrophages had an altered cytokine profile. The authors conclude that dietary pectin changed the T-helper (Th) cells phenotype to Th2, best suited to neutralization of bacterial toxins.

Prevention and Suppression of Cancer

Dried plums may exert a direct effect in the gastrointestinal tract, where the cells come in contact with all constituents, soluble and insoluble, absorbable and non-absorbable, and with bacterial metabolites of undigested prune constituents in the colon. Low fecal weight and slow bowel transit time are associated with increased risk of bowel and rectum cancer (Cummings et al., 1992). There is a significant correlation of dietary fiber intake with stool weight. Dried plums may help to prevent colon cancer due to their high content of fiber and sorbitol, which decrease colonic transit time and dilute fecal bile acids by increasing fecal output, and of phenolic compounds, which may act as antioxidants, preventing DNA damage in colonic epithelium. Binding of bile acids in the intestinal lumen by dietary fiber and other plant constituents may lower plasma cholesterol and aid the excretion of cancer-promoting secondary bile acids. This proposition was studied in vitro using freeze-dried powders prepared from fresh plums (unknown variety) and dried plums (Kahlon and Smith, 2007). The samples were digested with appropriate enzymes in a sequence imitating the natural digestion process, with a mixture of bile acids. Cholestyramine was used to provide a positive control (100% binding). Both fresh plum and dried plum powders bound bile acids better than other fruit powders (except blueberries).

Animal Studies

Colon cancer risk factors were studied in rats fed with dried plum powder diets (4.75% and 9.5%) and injected with azoxymethane, a known carcinogen, to induce the formation of pre-cancerous lesions, referred to as aberrant crypt foci, in the colon (Yang and Gallaher, 2005). There were two control groups, one fed with a basal diet, and the other a carbohydrate-matched diet, with added pectin, fructose, and glucose. There were no differences among the diets in the number of aberrant crypt foci after nine weeks of feeding. The collected fecal samples had lower concentrations of bile acids in dried plum powder-fed groups, and the daily excretion of bile acids was also decreased in those rats, although the differences were not consistently significant and dose-dependent. Colonic bacteria were isolated from cecal contents at the end of the experiment and their enzyme activities were assessed. Both 7α-dehydroxylase (catalyzer of deoxycholic and lithocholic acids formation from primary bile acids) and β-glucuronidase activities were decreased in bacteria from dried plum powder-fed rats, but nitroreductase activity was greatly increased. The lower 7α-dehydroxylase activity indicates that the dried plum powder diet may alter colonic bacteria, decreasing their capacity to produce cancer-promoting secondary bile acids. The other two enzymes are controversial because they may liberate some carcinogens or inactivate them, as well as liberate beneficial phytochemicals, depending on the substrate. The ORAC value of dried plum powder was measured, as well as the ORAC value of cecal contents. Compared with the basal diet, a low dose of dried plum powder doubled the ORAC value of cecal content (per milliliter), the high dose tripled it, while carbohydrate-matched diet did not have any effect. Therefore, the dried plum powder had favorable effects on antioxidant capacity within the colonic contents, and possibly decreased the production of cancer-promoting compounds by colonic bacteria. The duration of the experiment was too short to permit the assessment of the development of colon tumors from aberrant crypt foci. However, in a similar experiment with 5% freeze-dried fresh plums (unknown variety) in the diet, there was a very substantial decrease (86%) in the total number of azoxymethane-induced aberrant crypt foci (Boateng et al., 2007), and especially in large foci with more than four crypts, which are more likely to develop into tumors. Hepatic glutathione-S-transferase activity was 2.4-fold higher in the plum-fed rats, compared with the control diet. It is one of the phase-II metabolizing enzymes and its induction by plum phytochemicals may facilitate elimination of xenobiotics and carcinogens from the body.

Cell Culture Studies

In experiments with cell cultures, the extracts from concentrated prune juice (125 and 250 μg/mL) reduced viability of a human colon cancer cell line (Caco-2) and stomach carcinoma (KATO III) cells, but not that of normal colon fibroblasts (Fujii et al., 2006). An increased apoptosis was observed in Caco-2 cells incubated with 250-μg/mL extract concentration. However, 1-mM chlorogenic acid (354 μg/mL) had no effect on the viability of Caco-2 cells. Fresh plum (*P. domestica*, cv Arbuznaja) extracts inhibited proliferation of human colon cancer cells HT29 at 0.05–0.5% concentration (Olsson et al., 2004). The same group investigated proliferation of breast cancer cell line, estrogen-dependent MCF-7, and found similar, but slightly less pronounced effect. Another study evaluated the effect of plum extract and various phenolic fractions on the proliferation of both MCF-710A (estrogen dependent) and estrogen-independent MDA-MB-435 breast cancer cells, along with normal breast epithelial MCF-10A cells (Norrato et al., 2009). Plum extract was most effective in suppression of proliferation in estrogen-independent breast cancer cells, while estrogen-dependent cancer calls were most resistant. Among phenolic fractions of plum extract, flavonol (quercetin glucoside and rutinoside) and proanthocyanidin fractions were most active. The phenolic acid fraction inhibited proliferation of normal breast epithelial cells to a lesser degree than other fractions. Pure chlorogenic acid and neochlorogenic acid inhibited MDA-MB-435 cell growth by 50% (IC_{50}) at 17 μg/mL and 10 μg/mL, respectively, but did not suppress normal cell or MCF-7 cell proliferation up to 60 μg/mL. These concentrations are of the order found in plasma of healthy volunteers (6 μg/mL) after ingestion of green coffee extract (Farah et al., 2008). Chlorogenic acid shows cytotoxicity against human oral tumor cell lines, oral squamous cell carcinoma (HSC-2), and salivary gland cancer (HSG), but normal human gingival fibroblasts are much more resistant ($IC_{50} = 1.4$ and 1.3 mM vs 2.3 mM, respectively; Jiang et al., 2000).

Immature fruits of Japanese plum (*Prunus salicina* Lindl.) contain a higher level of total phenolics and proanthocyanidins than mature fruits, so their extracts were used on six different human cancer cell lines: Hep G2 (liver), Hela (cervical), U937 (leukemia), KATO III (stomach), MCF-7, and MDA-MB-231 (Yu et al., 2007). The extracts were strongly cytotoxic at 0.5 mg/L and 1.0 mg/L concentrations for all cell lines except MCF-7, while estrogen-independent breast cancer line MDA-MB-231 was most susceptible due to a very high rate of apoptosis (67% at the extract concentration of 0.1 mg/L).

Heterocyclic amines, produced during cooking meat, are carcinogenic in laboratory animals, but fruit and vegetable consumption may have a protective effect, especially for the epithelial cells of digestive tract. Genotoxic effects of 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP), the most abundant heterocyclic amine, were investigated in Chinese hamster lung fibroblast cultures, made susceptible by genetic engineering (Edenharder et al., 2002). The application of fresh plum homogenate reduced PhIP-induced DNA damage, assessed by the comet assay, at concentrations similar to red wine or red grape homogenate.

Human Studies

Since high intakes of fruits and fiber are associated with lower incidence of breast cancer, the effect of dried plum

consumption on estrogen metabolism was investigated in 19 healthy premenopausal women (Kasim-Karakas et al., 2002). The subjects consumed their usual diet for three menstrual cycles, and dried plums (100 g/day) for the next three menstrual cycles. Sex steroid hormone metabolites were assessed in their urine every day. There was a significant decrease in the excretion of the estrogen conjugates, 2–hydroxyestrone and 16α-hydroxyestrone, during the luteal phase on the dried plum diet, but their ratio did not change. The first conjugate is biologically inactive and does not promote estrogen-dependent breast cancer, while the second is considered a risk factor. A high ratio of the inactive metabolite to the active metabolite is considered protective against breast cancer.

The presence of inositol in dried plums and their products may contribute to their protective effects, especially in cell culture and animal experiments. Supplemental inositol was found to reduce dysplastic bronchial lesions in smokers (Lam et al., 2006), albeit at a high dose of 18 g/day. Unexpectedly, it also reduced their blood pressure after one month of treatment.

The above-described experiments with laboratory animals and cell cultures indicate that dried plums may be protective against many forms of cancer due to their high fiber content and various phytochemicals, which may trigger diverse mechanisms of detoxification of endogenous and exogenous cancer promoters. Admittedly, many experiments used high concentrations of phytochemicals that may not be physiologically feasible to maintain in tissues, except in the epithelium of gastrointestinal tract.

Diabetes and Atherosclerosis

According to the new international table of glycemic index (GI) (Foster-Powell et al., 2002) dried plums may be classified as a low-GI food (GI = 29 $\pm$ 4). Ten healthy subjects were checked for blood glucose response two hours after consuming pitted California dried plums (60 g serving, containing 33 g of available carbohydrates), or glucose. Calculated GI against white bread was 41, and the glycemic load of such serving was 10 (available carbohydrates multiplied by GI/100). Another determination of GI used larger servings of dried plums (97 g and 123 g), and calculated that the larger portion contained 50 g available carbohydrates (Glycemic Index Testing Inc., 2004). The values of GI were 49 for dried plums and 30 for prune juice. According to the classification proposed by Miller, low GI values are less than 55 (Foster-Powell et al., 2002). Low-GI foods are more satiating than high-GI foods, and do not cause large postprandial rise and fall in blood insulin. Therefore, low-GI foods are recommended for managing diabetes and for weight control. The high content of sorbitol in dried plums may be partly responsible for their low GI. Sorbitol has a very low GI of 9, and a meal composed of glucose and sorbitol yielded a glycemic load smaller than predicted from the sum of individual loads, possibly due to decrease of glucose absorption in presence of sorbitol (Livesey, 2003).

Dried fruit consumption (at least 1 oz/day) was associated with reduced abdominal obesity and reduced the risk of being overweight or obese (BMI > 25 kg/m^2) in adults, as seen in the NHANES, 1999–2004 population data base (Keast and Jones, 2009). The short-term effect of the addition of dried plums to a snack was studied in 45 healthy, normal weight subjects (Farajian et al., 2010) in a controlled laboratory setting. The subjects ate a standardized breakfast and two hours later took a snack of bread, cheese, and five dried plums. Three hours later they received lunch and dessert, consumed ad libitum. The experiment was repeated with the same subjects receiving an equicaloric snack of bread and cheese. The subjects had significantly smaller energy intake during lunch when dried plums were included in the snack, and ate less dessert (chocolate cake). Their feeling of satiety was higher at all points between the snack and lunch. Dried plums were also evaluated against low-fat cookies in 19 fasting adult women who ate them as a snack two hours before a test meal (Furchner-Evanson et al., 2010). The rise of plasma glucose and insulin after the dried plum snack was lower than after cookies and the satiety index was higher. In another study by the same group (Howarth et al., 2010), 29 women had two snacks daily for two weeks, consisting of dried plums (100 kcal, 42 g servings), and equicaloric snacks of low-fat cookies for another two weeks (randomized, crossover trial with washout period). Plasma triglycerides were significantly lower after dried plum consumption than after cookies, and the intake of fiber, potassium, riboflavin, niacin, and calcium was significantly greater.

In the Los Angeles Atherosclerosis Study (n = 500), a significant association was observed between the progression of atherosclerosis (measured ultrasonographically by the intima-media thickness of carotid arteries) and the intake of pectin (Wu et al., 2003). Triglyceride levels and the ratio of total cholesterol to HDL–cholesterol were inversely related to the total fiber intake, assessed by repeated dietary recalls.

Another component of dried plums, chlorogenic acid, significantly lowered plasma concentrations of cholesterol and triglycerides when infused intravenously into obese, hyperlipidemic, and insulin-resistant rats (Rodriguez de Sotillo and Hadley, 2002). The rats were infused with chlorogenic acid (5 mg/kg BW/day) or saline solution for three weeks. The control rats gained two-fold more weight during this time than the treated rats. There was a significant decrease in the liver triglycerides of chlorogenic acid-infused rats and their postprandial peak of blood glucose was significantly reduced.

Early in vitro experiments with chlorogenic acid indicated that it may decrease glucose active transport across intestinal brush border and inhibit production of glucose in the liver fractions (reviewed by Stacewicz-Sapuntzakis et al., 2001). More recent experiments on human intestinal Caco-2 cells found that apple extracts decreased glucose uptake and transport in Caco-2 cell monolayers due to the presence of polyphenols and phenolic acids (Manzano and Williamson, 2010). The apple extracts contained considerable concentration of chlorogenic acid (0.33 mM), which was found responsible for 12% of glucose transport inhibition activity.

A trial with healthy volunteers consuming glucose with caffeinated or decaffeinated coffee, both containing 354-mg chlorogenic acids, suggested that caffeine in coffee may impair glucose tolerance, while chlorogenic acids have the opposite effect (Johnston et al., 2003), as indicated by gastrointestinal hormone profiles. These incretin hormones were assayed in blood samples along with glucose and insulin, and their kinetics were consistent with delayed glucose absorption in the distal portion of small intestine after drinking decaffeinated coffee. A similar experiment with healthy subjects involved drinking a dose of 25 g sucrose with chlorogenic acid-enriched coffee product (∼600-mg chlorogenic acids), caffeinated or decaffeinated coffee, in a crossover design (Thom, 2007). Only the chlorogenic acid-enriched coffee significantly decreased plasma glucose elevation within two hours compared with control (sucrose solution in water). The same publication reports another study with 30 overweight subjects (BMI: 27.5–32 kg/m^2), who were drinking five cups a day of instant coffee or the chlorogenic acid-enriched coffee product (∼600-mg chlorogenic acids per day) for 12 weeks. The increased intake of chlorogenic acids was associated with a significant decrease in body weight (5.4 ± 0.6 kg) and body fat (3.6 ± 0.3%).

The addition of dried plum extract (25% w/w) to the diet of stroke-prone spontaneously hypertensive rats significantly decreased their systolic blood pressure after a five-week treatment, compared to basic diet (Negishi et al., 2007). Smooth muscle cells were isolated from the aorta of these rats, incubated with caffeic acid, and challenged with angiotensin II. Their superoxide content decreased to control levels (without angiotensin) due to caffeic acid treatment. Dried plum powder was used in a study of atherosclerosis in apolipoprotein E-deficient mice (Gallaher and Gallaher, 2009). These mice quickly develop atherosclerotic lesions on diet containing cholesterol and saturated fat. For 20 weeks, they were fed with a basal diet, cholesterol diet (0.15%), and cholesterol diet with 4.75% or 9.5% dried plum powder. There was no effect of dried plum treatment on plasma cholesterol or triglyceride concentrations compared to cholesterol diet, but the atherosclerotic lesions in the aortic arch and arterial trees were significantly reduced by the lower dose of dried plum powder. Serum amyloid P-component (SAP), a systemic marker of inflammation in mice, was doubled in cholesterol-rich diet group, but the effect of cholesterol disappeared when dried plum powder was added. Interestingly, the higher dose was not more effective than the lower dose for any measured parameter in this study.

Similar studies with other species of plums (Asian apricot *P. mume* and Japanese plum *P. salicina*) deserve consideration, although relative proportions of various phytochemicals in these fruits differ from dried plums (*P. domestica*), and the experiments were conducted with fresh fruit extracts or concentrated juice. When insulin-resistant obese rats and diabetic mice were given Asian apricot juice concentrate (*ekisu*, made from the fruit of *P. mume*) in drinking water, their glucose tolerance improved significantly after two weeks of treatment (Utsunomiya et al., 2005). Their plasma levels of adiponectin increased, and mRNA expression of PPARγ in adipose tissue was enhanced. The treatment prevented the rise of total plasma cholesterol and triglyceride during the treatment, which occurred in the untreated obese rats. The same juice concentrate inhibited in vitro the angiotensin II-induced protein synthesis in vascular smooth muscle cells prepared from the aorta of normal rats (Utsunomiya et al., 2002). It may indicate a protective action of *ekisu* against vascular hypertrophy and high blood pressure. Phenolic extracts from Black Splendor plum (*P. salicina*) were effective in decreasing oxidative stress induced by 10-mM glucose in human umbilical vein endothelial cell cultures (Townsley et al., 2009) as indicated by the decrease in inflammatory biomarkers IL-6 and IL-8 and transcription factor NF-κB.

Oxidized lipids engulfed by macrophages in endothelial walls produce atherosclerotic plaque. When mouse macrophages RAW264.7 were stimulated in vitro with $FeSO_4$ and H_2O_2, the extracts of dried plum phenolics reduced their malonaldehyde production (an indicator of lipid peroxidation) (Kumar et al., 2009).

Iron Absorption

High content of phenolic compounds in fruit juices inhibits the intestinal iron uptake by forming irreversible complexes, while ascorbic acid promotes iron absorption. Among different fruit juices, red grape and prune juices were found to inhibit the absorption of soluble iron in Caco-2 cell model combined with in vitro digestion (Boato et al., 2002). Caco-2 cell ferritin formation was used as the marker of iron uptake and it decreased 31% by prune juice and 67% by red grape juice. Although the effect of prune juice was not statistically significant, the authors' suggestion was to limit the intake of both juices in infants and in other conditions of iron insufficiency, but to increase it for people at risk of hemochromatosis. There are some indications that many degenerative diseases, as well as the toxicity of many compounds, involve poorly bound iron, producing hydroxyl radicals (Kell, 2010). Therefore, iron-chelating dietary compounds present in dried plums may prevent or inhibit the progression of cellular insults caused by iron overload.

Neurologic and Psychiatric Effects

Recent experiments with aging laboratory animals indicated that high intake of various fruit or vegetable extracts were effective in reversing neurochemical and behavioral changes associated with decline in cognitive performance. Dried plum powder and plum juice prepared from fresh prune-making plums were used in a study of 19-month-old rats (Shukitt-Hale et al., 2009). The animals were already showing neurologic decrements by 15 months of age. One group of rats had dried plum powder added to a standard diet at 20 g/kg (2%), while another group was drinking plum juice instead of water. Both groups and control groups were tested after eight-week treatment using the Morris water maze, where they learned to find a submerged platform in a circular pool. Latency (time to find the platform) and the

Table 13 Potential health effects of dried plum components

	Potential health effects								
Dried plum components	Laxative	Gastrointestinal	Anti-cancer	Cardiovascular	Anti-diabetic	Bone	Anti-bacterial	Immune function	Neural & cognitive
Dietary fiber	•	•	•	•	•			•	
Sorbitol	•	•	•	•	•	•	•		
Inositol									•
Phenolic compounds	•	•	•	•	•	•	•	•	•
Quinic acid							•		
Vitamin K1				•	•	•			
Boron					•	•			•
Copper				•	•	•			
Potassium				•		•			

distance traveled to find it were the measures of improved working memory. Both measures were significantly shorter for plum juice-drinking rats, which indicated improvement of memory and faster learning. The dried plum powder diet had no effect on cognitive performance, possibly because it delivered much less antioxidants than plum juice (3.3-mg GAE/day vs 30.3-mg GAE/day), and some antioxidants are destroyed during the preparation of dried plum powder, which is more extensive than that of plum juice. Serum of rats consuming plum juice had significantly higher ORAC values, while that of dried plum powder-treated rats was not different from the controls.

The main constituent of dried plum phenolics, chlorogenic acid, was investigated in mice using exploratory tests for anxiety and neophobia (Bouayed et al., 2007). However, chlorogenic acid was injected intraperitoneally, bypassing absorption and colonic degradation. At 20 mg/kg BW chlorogenic acid caused a decrease in anxiety-related behavior, i.e., the treated mice were more likely to investigate unfamiliar and well-lit environment. Previously, the same group found that there is positive correlation between peripheral blood granulocyte oxidative status and level of anxiety in mice. Therefore, they used mice granulocytes to evaluate the chlorogenic acid effect on oxidative stress generated by the addition of H_2O_2 in vitro and found that 0.5-mg chlorogenic acid was equivalent to 0.12 mg of vitamin C.

Interestingly, serotonin, a neurotransmitter, which decreases anxiety and neophobia, was found in red, blue–red, and blue plums of unspecified varieties (3.6–5.7 μg/g; Feldman and Lee, 1985), but there are no data for dried plums. Serotonin is well absorbed into circulation, but apparently cannot cross brain blood barrier, so the ingested serotonin should not affect the behavior and cognition. Another component of dried plums, inositol, has been investigated in treatment of various psychiatric disorders (Levine, 1997). Inositol is a source of several second messengers in brain and its content is reported to be decreased in cerebrospinal fluid in depression. Significant therapeutic effects of inositol supplementation were found in depression and panic disorder (dose of 12 g/day), and in obsessive-compulsive disorder (18 g/day). Inositol was not helpful in schizophrenia, Alzheimer's disease, attention deficit disorder with hyperactivity in children, autism, or electroconvulsive therapy-induced memory impairment. All trials had a double-blind crossover design with placebo (glucose) and included 9 to 28 patients. The investigators concluded that inositol may be beneficial in diseases responsive to serotonin selective re-uptake inhibitors. An increased dietary intake of inositol may also have a therapeutical potential in the treatment of diabetic neuropathy, delaying the onset or improving sensory nerve function. Such improvement was reported in 20 diabetic patients when the total mean daily intake of inositol was increased from 0.77 to 1.65 g/day (Clements, 1980). According to the data in Table 2, moderate servings of dried plums or prune juice could deliver physiologically significant amounts of inositol.

High-antioxidant fruit extracts were also found to decrease the toxic effects of dopamine or amyloid β-peptide in transfected COS-7 cell model (Joseph et al., 2004). Dried plum (0.5 mg/mL) extract significantly improved viability of dopamine-treated cells and regulation of calcium fluxes in amyloid β-peptide-treated cells. The authors surmised that fruit intake may provide some protection against neuronal aging and Alzheimer's disease.

SUMMARY AND FURTHER RESEARCH RECOMMENDATION

During the last decade (2000–2010) there has been a considerable progress in discovering and understanding of health effects related to the consumption of dried plums. Table 13 attempts to summarize the possible effects in the form of a grid, although more accurate representation may be that of a complicated web, since many health effects are interrelated and the dried plum components may act in synergy. Increasingly, health professionals are urged to focus on whole foods, rather than individual nutrients (Mozzaffarian and Ludwig, 2010), as dietary targets in order to design more effective strategies for the prevention of chronic diseases. Dried plums are a whole, minimally processed food, belonging to a traditional, time-tested way of eating in many populations. Recent studies on replacing other snacks with dried plums indicate many beneficial health effects besides increasing satiety and reducing desire for sweetened

Table 14 Future research recommendations

Composition studies
- Assessment of all constituents of fresh prune-making plums to investigate changes occurring during processing by comparing fresh and dried plums.
- Assessment of individual sugars, vitamin B_6, and iron in prune juice (discrepancy in USDA SR 25 with the data inferred from dried plums).
- Analysis of phenolic compounds in fresh plums d'Agen, dried plums, and dried plum powder using phloroglucinolysis and/or thiolysis to assess proanthocyanidins content and type.
- Assessment of serotonin content in dried plums and prune juice.

Cell culture studies
- Experiments on the cells of gastrointestinal tract (normal and cancer cell lines, preferably human) with extracts and homogenates of dried plums (viability, absorption of nutrients and bioactive compounds).
- Experiments on the cells involved in bone maintenance, atherosclerosis, diabetes, various cancers, or cognition, with identified metabolites of dried plum phenolic compounds.
- In vitro experiments with urine of animals or humans on dried plum diet: assessment of bacteriostatic action of urine on UTI-causing strains and their adhesion to urinary epithelial cells, hippuric acid, and other metabolites of dried plum constituents in urine.
- In vitro study of *H. pylori* suppression and adhesion to stomach epithelial cells or gastric mucus by prune juice or dried plum homogenates.

Animal studies
- Repetition of animal experiments involving bone preservation, cognitive decline, immune response, atherosclerosis, and cancer with diet containing a powder made of dried plums by technologies less destructive to antioxidants, or prune juice replacement of drinking water.
- Animal experiments on absorption of iron while drinking prune juice (assessed for the content of iron, vitamin C, and phenolic compounds) with a control diet or drink containing the same amount of iron and vitamin C. Blood iron parameters should be measured and compared in both groups.

Human studies
- Intervention trial of a few healthy subjects on controlled diet to study the metabolism of phenolic compounds from dried plums: a washout period of commercial liquid diet and water, followed by a period of liquid diet and dried plums (100 g/day) with collection of blood samples, urine, and feces for analysis.
- Intervention study to check production of nitric oxide in stomach and changes in colonic flora after eating dried plums or drinking prune juice.
- Intervention trial (crossover design) of subjects prone to UTI with a daily supplement of dried plums or prune juice (negative control – no dietary intervention; positive control – cranberry juice or sauce), and collection of urine samples for in vitro experiments and analysis.

food, very important factors in controlling overeating, obesity, diabetes, and related cardiovascular diseases.

Dried plums contain unique constituents in characteristic amounts and proportion, which are not found in common foods, even in other dried fruits. These are listed in Table 13, while other tables report their content in dried plums and their products. The combination of dietary fiber, sorbitol, and chlorogenic acids may be responsible for many beneficial gastrointestinal effects, including prevention of constipation, dental caries and gingivitis, stomach ulcers, and colon cancer. The metabolites of quinic acid and specific phenolic compounds (chlorogenic acids and proanthocyanidins) may also act as bacteriostatic agents in prevention of UTI. Phenolic compounds are implicated in all listed potential health effects, including anti-diabetic action, cardiovascular benefits, bone preservation, improved immune function, and mitigating neural/cognitive defects. The relatively high content of phylloquinone (vitamin K1) may be important for cardiovascular health, bone metabolism, and glucose/insulin regulation, working synergistically with boron and copper, which are also abundant in dried plums. Western diet is characterized by low intake of potassium and overly high intake of sodium, especially from processed foods, therefore potassium content of dried plums may be beneficial for cardiovascular system and bone maintenance. The presence of inositol may also aid cardiovascular health, as well as neural and cognitive function.

Much progress was recently achieved in the investigation of therapeutic effects of dried plums on bone turnover, with numerous mechanistic studies on animals and cell cultures. However, it is still unknown which individual compounds, alone or in combination, produce the observed effects. The presence of phenolic metabolites in circulation is still very controversial, with some researchers finding significant concentrations of possibly active metabolites of chlorogenic acids and others reporting negative results. The difficulties of measuring phenolic compounds are also encountered in the analysis of dried plum, with unresolved question of proanthocyanidin content, which are possibly a major fraction. The problem of physiologically significant concentrations of active metabolites reaching target tissues is of vital importance in the investigation of potential preventive and therapeutical effects.

In conclusion, this review summarizes further research recommendations in Table 14, in hope that it will help the researchers to direct their investigations on the elucidation of health effects of dried plums.

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Addendum

After completion of the preceding manuscript, an important study on mineral and vitamin content of dried fruits has been published in 2011 (Bennett et al., 2011). Dried plums d'Agen originated from three different countries, Australia, Chile and

the U.S. Some of the results are shown in the table below. Comparative values from USDA, 2012 (SR 25) are also included.

Micronutrient per 100 g dried plums	Australia	Chile	California, USA	USDA, 2012 SR 25
B, mg	2.04	3.18	1.96	
Ca, mg	42.9	38.8	37.2	43
Cu, mg	0.37	0.30	0.27	0.28
Fe, mg	3.18	2.08	2.12	0.93
K, mg	746.6	815.0	766.0	732
Mg, mg	32.9	39.8	41.3	41
Mn, mg	0.96	0.92	0.90	0.30
P, mg	57.2	79.4	72.9	69
Se, mg	0.00	0.24	0.00	0.3
Zn, mg	1.15	0.43	0.32	0.44
Folate, μg	29.7	21.8	19.8	4

Adapted from Bennett et al., 2011.

It is interesting to notice the high zinc content in Australian dried plums (10% DRI, see Table 3). The results for iron and manganese in the U.S. dried plums were much higher than reported in SR 25, and would deliver 12% and 39% DRI, respectively, in a 100 g serving. While vitamin C was not detected in any of the samples, folate content was quite high (5 -7.5% DRI). It is possible that the difference is due to the methodology employed for the determination of folate in dried plums, although it seems that microbiological methods were used in both investigations (Bennett et al., 2011 and USDA, 2012). Microbiological assays of folate are prone to very high inter-laboratory variability, therefore the direct HPLC analysis is much recommended (Koontz et al., 2005). Repeated analysis of iron and manganese should also be conducted.

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