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Effects of 12 Months Consumption of 100 g Dried Plum (Prunes) on Bone Biomarkers, Density, and Strength in Men

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ABSTRACT Several male animal studies have demonstrated bone-protective effects of dried plum; however, no human male study has evaluated the effect of dried plum on bone health. We conducted a randomized controlled clinical study to test if daily inclusion of 100 g of dried plum in the diet positively influenced bone mineral density (BMD), bone strength, and bone biomarkers in men. Sixty-six men were randomly assigned to one of two daily treatment groups: (1) control (0 g dried plum) or (2) 100 g dried plum. Blood samples were collected at baseline and after 3, 6, and 12 months to assess bone biomarkers. Bone was measured at baseline and after 6 and 12 months via dual-energy X-ray absorptiometry and peripheral quantitative computed tomography. Tartrate-resistant acid phosphatase-5b (TRAP5b) and C-terminal collagen cross-link (CTX) levels decreased significantly in the dried plum group at 3-, 6-, and 12-month intervals compared with baseline. No changes were observed in the control group for TRAP5b and CTX levels. Bone-specific alkaline phosphatase levels decreased significantly after 6 and 12 months in the control and dried plum groups. BMD for total body, spine (L1–L4), hip, and ulna did not change in the control and dried plum groups from baseline to 6 or 12 months. In the proximal tibia, endosteal circumferences increased significantly within the dried plum group during the course of treatment. The results suggest that daily consumption of 100 g dried plum for 12 months has modest bone-protective effects in men.
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KEYWORDS: • *fruit* • *osteopenia* • *osteoporosis*

INTRODUCTION

Osteoporosis is a progressive metabolic bone disease characterized by reduced bone mass and destructive bone microstructural changes resulting in bone fragility and increased fracture risk.[1] This is a significant health concern that is currently estimated to affect more than 54 million people in the United States, and its incidence is increasing due to the aging of the population.[2] About 47% of men older than 50 years have osteopenia, and men are 10–25% likely to experience at least one osteoporosis-related fracture in their lifetime.[2,3] Typically thought of as a disease impacting women, increasing attention is being paid to osteoporosis in men; however, little research has been conducted to address this situation. Men have higher morbidity and mortality associated with osteoporotic fractures compared with women.[4]

Currently, the prevention and treatment of osteoporosis involve pharmaceuticals that are costly, have significant side effects, and may not be effective, all of which fosters poor compliance.[5] This has encouraged a search for alternative nonpharmacological interventions for both prevention and treatment of osteoporosis. Of these, dried plums have shown potential in preventing bone loss.[6–8] Bone-protective properties of dried plum have been demonstrated in ovariectomized[9,10] and orchidectomized[11,12] animal models of osteoporosis and in postmenopausal women.[6,13] The beneficial effects of dried plum were also tested on male young adult mice with normal bones versus old mice with bone loss. The results demonstrated that dried plum increased bone volume above basal levels by nearly 50% in the young adult mice and 40% in the old mice. Dietary dried plum not only prevented bone loss but also replaced bone that had already been lost due to aging. The magnitude of the changes in bone volume was similar to those in gonadal hormone-deficient male (+36%) and female (+50%) rats fed diets supplemented with dried plum.[11] The effects of the dried plum diet were greatest in the young adult mice, suggesting that although both adult and old mice can respond to dried plum, the effects are somewhat blunted in the aged mice. In almost all cases, the response of adult mice to lower doses of dried plum was similar to the response to higher doses of dried plum, whereas old mice showed little or no response to lower doses of dried plum.[14]

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Although several studies in animals and women have demonstrated bone-protective effects of dried plum, no human study has evaluated the effect of dried plum on bone metabolism in men. Hence, the present study was designed to determine if consuming 100 g of dried plum per day can be effective in preventing loss of bone mineral density (BMD) and strength and improving bone biomarkers in men 50–79 years. We hypothesized that consuming 100 g of dried plum during calcium and vitamin D supplementation for 1 year would improve bone density, bone strength, and bone biomarkers compared with a control group consuming the calcium and vitamin D supplements only.

MATERIALS AND METHODS

Participants

A total of 66 healthy, normal weight male volunteers, aged 50–79 years, were recruited from the greater San Diego, California area. Recruitment took place in the community via flyers at local gyms, private medical offices, social media, and by word of mouth. Inclusionary criteria included being of male sex, between the ages of 50–79 years, and willingness to consume 100 g/day dried plum for 1 year. Exclusionary criteria included heavy cigarette smoking (more than 20 cigarettes per day); body mass index (BMI) <18 or >30 kg/m^2; <50 or >79 years old; diagnosis of bone, parathyroid, respiratory, or renal disorder problems; current or prolonged intake of medications affecting bone; regularly consuming dried plum or prune juice; and allergies to dried plum. Complete medical histories and a dietary vitamin D and calcium questionnaires (Short calcium and vitamin D questionnaire 2002) were obtained from the participant before initiating the treatment. The participants were advised to maintain their usual physical activity and diet pattern throughout the study.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human participants/patients were approved by the San Diego State University Institutional Review Board (No. 2521098). Written informed consent was obtained from all participants. The clinical trial is registered at ClinicalTrials.gov

Study design

Sixty-six men were randomly assigned to one of two treatment groups for 12 months: 100 g/day of dried plum ($n = 33$) and a control group of 0 g/day of dried plum ($n = 33$). Dried plum was provided in two sealed portions totaling 100 g/day. Participants were instructed to consume dried plum as they preferred at any time of the day and either in divided doses or in its entirety. The amount of dried plum was based on the findings of a long-term clinical trial with female humans,[6] which demonstrated that consumption of 100 g of dried plum per day for 12 months significantly improved bone health compared with the control group. To avoid any potential laxative effects, participants were instructed to gradually increase their consumption of dried plums in the span of 1 week culminating with consumption of 100 g/day. The composition of dried plum per 100 g obtained from Food Processor SQL Software (version 10.12.0, 2012; ESHA Research, Salem, OR, USA) is as follows: 240 calories, 0.38 g fat, 63 g carbohydrate, 2.18 g protein, 7.1 g fiber, 43 mg calcium, 0.93 mg iron, 41 mg magnesium, 69 mg phosphorous, 732 mg potassium, 2 mg sodium, 0.44 mg zinc, 0.281 mg copper, 0.3 μg selenium, 39 μg vitamin A retinol activity equivalents, 394 μg beta carotene, and 59.5 μg vitamin K (phylloquinone). All participants received 500 mg calcium and 300 IU vitamin D (Shaklee, Pleasanton, CA, USA) for each day of the study. Participants were given calendars and were asked to record the days they missed consuming the study regimen on the calendars. Additionally, they were asked to return unused portions of the regimen (dried plum and calcium/vitamin D supplements) to monitor compliance.

Dietary and physical activity assessment and anthropometric measurements

A medical history questionnaire was obtained during the baseline visit. Participants also completed a 3-day food record at baseline and after 3, 6, and 12 months. Dietary analysis was performed using Food Processor SQL Software (version 10.12.0, 2012). In addition, physical activity was assessed at baseline and after 3, 6, and 12 months using the Five City Project validated questionnaire.[15] Height was assessed at baseline and 12 months, and weight was determined during of the four visits. These anthropometric data were then used to calculate BMI (kg/m^2). Characteristics of the study participants are displayed in Table 1.

Serum bone biomarker measurements

Venous blood samples were obtained after an overnight fast from each participant at baseline and after 3, 6, and 12

Table 1. Baseline Characteristics of the Study Participants

Measure	*Control group (n = 33)*	*Dried plum group (n = 33)*
Age (years)	62.0 ± 12.9	62.1 ± 13.1
Height (baseline, cm)	178.7 ± 7.7	175.5 ± 6.5
Weight (baseline, kg)	87.6 ± 15.0	85.6 ± 12.8
Weight (12 months, kg)	87.1 ± 15.0	86.1 ± 13.1
BMI (baseline, kg/m^2)	27.3 ± 4.2	27.6 ± 3.6
T-score (L1–L4; baseline)	0.5 ± 1.7	0.2 ± 1.6
PA (baseline, kcal/day)	683 ± 214	531 ± 355
Vitamin D intake (baseline, μg)	5.0 ± 3.7	4.4 ± 3.1
Calcium intake (baseline, g)	0.92 ± 0.50	1.03 ± 0.43
Supplement calcium (g)	0.03 ± 0.07	0.08 ± 0.19
Dietary calcium (g)	0.89 ± 0.48	0.95 ± 0.34

Data are presented as mean ± SD. Control group: calcium and vitamin D supplement; dried plum group: calcium and vitamin D supplement and 100 g/day dried plum. The Five-City Project Physical Activity recall was used to assess current PA, sleep, and activity pattern including leisure, occupation, and home activities. There were no statistically significant differences observed between the baseline values of the two groups and between the baseline and corresponding values for weight at 12 months.

BMI, body mass index; PA, physical activity; SD, standard deviation.

months of the study. Blood samples were centrifuged at 1200 *g* for 15 min at 4°C, and serum samples were divided into aliquots and stored at −80°C until analyzed. Baseline, 3-, 6- and 12-month samples were analyzed for changes in bone-specific alkaline phosphatase (BAP) and tartrate-resistant acid phosphatase-5b (TRAP5b) levels using ELISA kits (Quidel Corporation, San Diego, CA, USA). Additionally, samples were analyzed for changes in N-terminal propeptide of type 1 procollagen (P1NP) and C-terminal collagen cross-links (CTX) and were measured by a luminescent immunoassay analyzer (ISYS Analyzer; Immunodiagnostics Corporation, Woburn, MA, USA). Finally, baseline and 12-month samples were analyzed for changes in vitamin D using ELISA kits (ALPCO, Salem, NH, USA). Intra-assay (within-run) and inter-assay (between-run) coefficients of variation (CV) were 5.0% and 7.5% for BAP, 2.2% and 3.0% for TRAP5b, 2.87% and 4.63% for P1NP, and 3.22 and 6.16 for CTX.

Bone densitometry assessment

Bone density was assessed via dual-energy X-ray absorptiometry (DXA; GE Healthcare Lunar, Madison, WI, USA) with software to analyze bone densitometry. Densitometer stability was evaluated by performance of phantom scans on the dates of all data acquisition. The precision of this technique, presented as the CV, was 0.70% for the lumbar spine, 0.75% for the total hip, 0.85% for forearm, and 0.65% for total body locations. Scans were completed for analysis of bone density at the total body, lumbar spine (L1–L4), dual femur, and nondominant forearm at baseline and after 6 and 12 months for each participant.

Peripheral quantitative computed tomography measurements

A single operator obtained peripheral quantitative computed tomography (pQCT) measurements (XCT-3000; Stratec Medizintechnik, Pforzheim, Germany) of the left tibia. Phantom scans were performed daily to verify the calibration of the XCT-3000. The operator performed scout view scans of the distal left tibia and established a reference point at the end plate. All sites were scanned with the following parameters: 0.4 mm pixel size and 20 mm/s scan speed. All sites were scanned at baseline and after 6 and 12 months of intervention. The Stratec XCT 6.00 software package was used for image analysis. At all sites, an region of interest was drawn to isolate the tibia. The 4% site was analyzed with a threshold of 169 mg/cm^3 and contour mode 3 and then peel mode 4 with an inner threshold of 650 mg/cm^3 and a 10% concentric peel to define trabecular. The distal sites of 38% and 66% used a threshold of 710 mg/cm^3 and cort mode 2 to define cortical bone for area and density measures. In addition, the distal sites were analyzed with cort mode 2 and a threshold of 480 mg/cm^3 to determine the stress–strain index.

Statistical analysis

Data were analyzed using analysis of variance methods with PROC MIXED in PC SAS (Version 9.1; SAS Institute, Cary, NC, USA) analyzing the main and interaction effects of the two factors, treatment (0 or 100 g/day dried plum) and time (baseline, 3, 6, and 12 months), for bone biomarkers. Bone density and strength were analyzed for main and interaction effects of two factors, treatment (0 or 100 g/day dried plum) and time (baseline, 6 and 12 months). The mean changes in each time point for the treatment groups were compared by analyzing interaction effects of the two factors, treatment and time, using the SLICE option in an LSMEANS statement. The differences at baseline between the two groups were assessed using independent *t*-tests. Data are reported as mean ± standard error or standard deviation; unless otherwise indicated, $P < .05$ was regarded as statistically significant.

RESULTS

Fifty-seven participants (32 assigned to 0 g/day dried plum and 25 assigned to 100 g/day dried plum) completed the 12-month study (Fig. 1). The attrition rate was 3.0% for the control group and 24.2% for the dried plum group. As expected, baseline characteristics were not significantly different for men who completed the study (Table 1). Age, height, body weight, and BMI were similar at baseline between the two treatment groups.

The 57 participants who remained in the study adhered to the regimens, as indicated by a self-monitoring calendar provided to them, as well as analysis of returned unused portions of the treatment regimen supplied to the participants. On average, the compliance to the control group regimen was 98.3%, and the compliance to the dried plum regimen was 93.8% for duration of the study. Intakes of habitual calcium and vitamin D were evaluated at baseline using calcium and vitamin D intake history questionnaires. There were no significant differences in calcium and vitamin D intake between the treatment groups throughout the study (Table 1).

Dietary data (Table 2) indicated that dried plum consumption promoted higher intake of carbohydrate, dietary fiber, vitamin A, vitamin K, and potassium in comparison to the control group. No other changes in nutrient intake over time or between the groups were detected. Physical activity was not significantly different in activity levels between or within the treatment groups (Table 3).

Serum BAP levels decreased significantly at 6 and 12 months in the control group and decreased significantly ($P = .001$) at 12 months in the dried plum group ($P = .001$; Table 4). One hundred grams per day dried plum consumption resulted in a time-dependent reduction in serum TRAP5b levels, a marker of bone resorption, at 3-, 6-, and 12-month intervals ($P = .003$) compared with baseline while there were no significant changes in serum TRAP5b levels for the control group (0 g/day dried plum). CTX, another marker of bone resorption, modestly decreased in the dried plum group at 3-, 6-, and 12-months compared with baseline ($P = .04$). No changes were observed in the control group for CTX levels. There were no changes in the control or dried plum groups for P1NP or vitamin D levels at any time intervals.

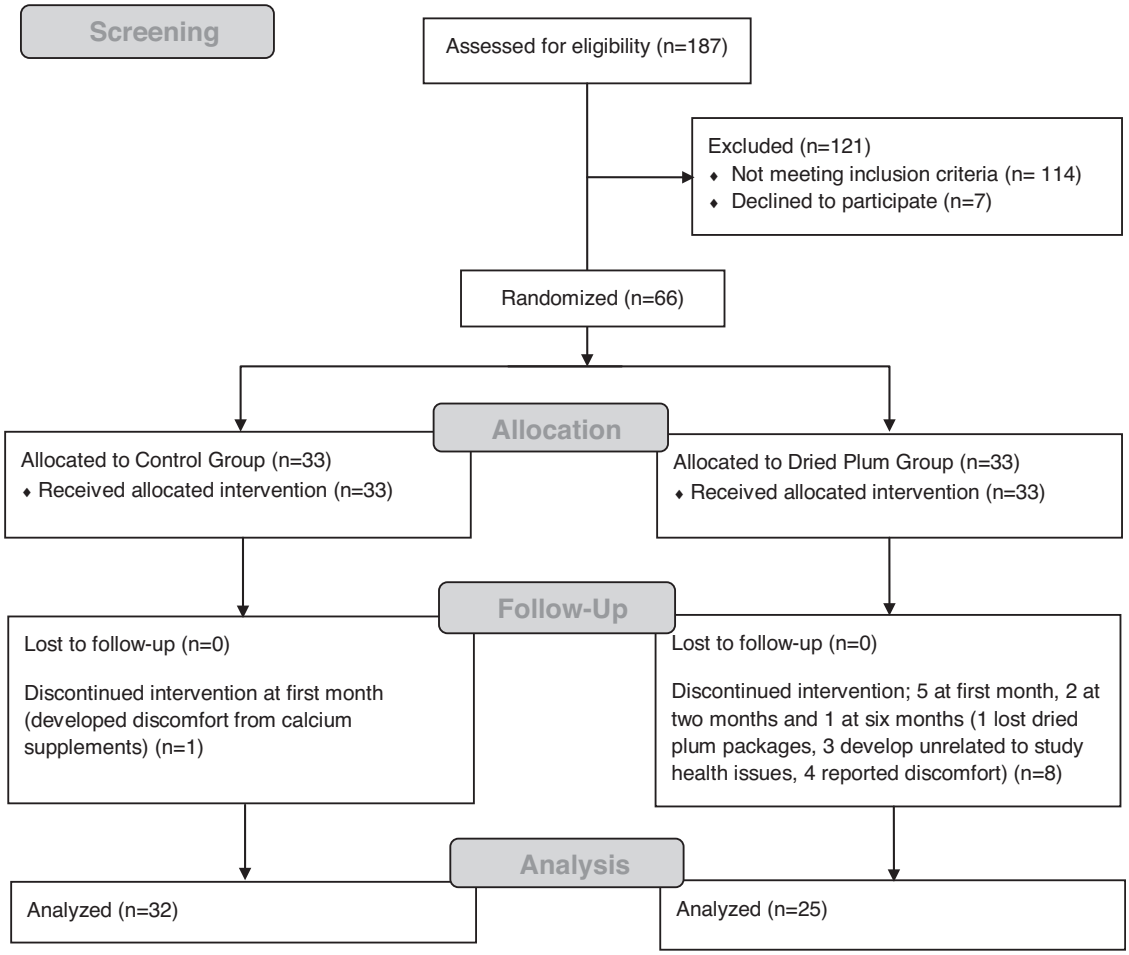

FIG. 1. Study flow diagram.

The mean BMD measurements are included in Table 5. There were no significant changes in BMD after baseline as assessed via DXA at either the 6- or 12-month time points for total body, ulna, lumbar spine, and dual hip sites within or between the two treatment groups.

At the 4% tibia site, there were no significant changes in the control group or the dried plum group from baseline compared with the 6- or 12-month visit (Table 5). There were no significant changes in total density, trabecular density, and bone strength index for the dried plum group. At the 38% tibia site, there was no significant change in any of the measured area or indexes. At the 66% tibia site, there was a significant interaction between time and group for total area, periosteal and endosteal circumference. Endosteal circumferences increased significantly in the dried plum group after 12 months. Although a time × group interaction failed to achieve statistical significance ($P = .057$), total density as assessed by pQCT increased by the 12-month time point for the dried plum group. Additionally, a trend ($P = .08$) for a main effect of increasing cortical thickness was detected over time. This effect was only statistically significant for the 12-month time point compared with baseline within those receiving dried plums.

DISCUSSION

The results of this study suggest that daily consumption of 100 g dried plum for 12 months has modest bone-protective effects in men. TRAP5b and CTX levels decreased significantly in the dried plum group at 3-, 6-, and 12-month intervals compared with baseline, whereas no changes were observed in the control group. BAP levels decreased significantly after 6 and 12 months in the control and dried plum groups. BMD as measured by DXA for total body, spine (L1–L4), hip, and ulna did not change in the control or dried plum groups. However, in the proximal tibia, endosteal circumferences increased significantly within the dried plum group during the course of treatment.

Previous studies confirm that dried plums promote bone in male and female animal models.[11,12,16] Daily dried plum consumption also prevented bone loss in osteopenic postmenopausal women regardless of dose (50 g vs. 100 g).[6] Results of those studies are to some degree consistent with the modest bone-protective effects observed in this study of men aged 50–79 years consuming 100 g of dried plum daily for 1 year. Specifically, decreased concentrations of both CTX and TRAP5b, established serum biomarkers of bone

Table 2. Daily Nutrient Intake Calculated from a 3-Day Food Record at Baseline, 3, 6, and 12 Months

	Control group				*Dried plum group*			
Daily intake	*Baseline*	*3 Months*	*6 Months*	*12 Months*	*Baseline*	*3 Months*	*6 Months*	*12 Months*
Total energy (kcal)	2224 ± 856	2094 ± 764	2288 ± 833	2224 ± 950	2188 ± 831	2338 ± 1012	2678 ± 1332	2305 ± 1035
Macronutrients								
Protein (g)	98 ± 50	94 ± 52	96 ± 40	90 ± 39	85 ± 27	85 ± 45	93 ± 41	86 ± 41
Carbohydrate (g)	235 ± 101	219 ± 106	264 ± 103	228 ± 92	264 ± 147	308* ± 145	411* ± 355	303* ± 131
Dietary fiber (g)	25 ± 14	23 ± 12	25 ± 13	25 ± 14	27 ± 14	31* ± 16	45* ± 45	32* ± 18
Total fat (g)	98 ± 55	86 ± 34	89 ± 42	103 ± 77	90 ± 39	81 ± 48	80 ± 35	88 ± 49
Vitamins								
A (μg RAE)	854 ± 485	601 ± 388	753 ± 513	828 ± 522	1104[a] ± 1019	670[a,b] ± 416	1264*,[a,c] ± 1070	1109*,[a] ± 961
C (mg)	289 ± 360	136 ± 90	206 ± 296	128 ± 111	217 ± 245	180 ± 133	206 ± 209	237 ± 473
D (μg)	5 ± 2	4 ± 2	5 ± 4	6 ± 9	6 ± 11	4 ± 3	4 ± 2	4 ± 9
E (mg)	5.7 ± 11.6	8.0 ± 10.0	5.8 ± 3.7	6.2 ± 3.7	4.2 ± 10.1	4.2 ± 7.7	4.2 ± 5.3	7.2 ± 4.2
K (μg)	141[a] ± 99	100[a,b] ± 77	159[a,c] ± 94	201[a] ± 314	155 ± 64	114 ± 94	377* ± 432	339* ± 242
Minerals								
Calcium (mg)	951 ± 551	993 ± 1060	1024 ± 397	888 ± 445	1169 ± 847	901 ± 831	1068 ± 457	1157 ± 884
Iron (mg)	29 ± 65	15 ± 9	18 ± 9	18 ± 12	17 ± 9	15 ± 11	18 ± 7	17 ± 8
Magnesium (mg)	396[a] ± 243	234[b] ± 176	470[a] ± 273	380[a] ± 195	514[a] ± 406	283[a,b] ± 192	495[a,c] ± 260	414[a] ± 213
Phosphorous (mg)	1376[a] ± 633	950[a,b] ± 912	1454[a,c] ± 565	1342[a] ± 518	1252[a] ± 409	817[b] ± 550	1434[a,c] ± 615	1331[a,b] ± 670
Potassium (mg)	3078[a] ± 1283	2289[b] ± 1274	3843[a,c] ± 2402	3450[a] ± 1762	3607[a] ± 2440	3244*,[a,b] ± 1559	5065[a,c] ± 4339	3679[a] ± 1429
Zinc (mg)	15 ± 11	14 ± 5	14 ± 9	15 ± 11	15 ± 8	14 ± 7	13 ± 6	12 ± 6

Data are presented as mean ± SD. Control group: calcium and vitamin D supplement; dried plum group: calcium and vitamin D supplement and 100 g/day dried plum. Means with the asterisk (*) are significantly different between the groups, $P < .05$. Means with different superscript letters are significantly different within group, $P < .05$. Both groups were supplemented with 50% daily value of calcium and vitamin D, and analysis include calcium and vitamin D supplements used by the participants.

RAE, retinol activity equivalents.

resorption, were detected in the dried plum treatment cohort. These results also corroborate previous studies of dried plum supplementation in postmenopausal women that reflect an attenuation of bone resorption markers.[6,8] With regard to biomarkers of bone formation, no change within either group for P1NP were detected; however, BAP decreased in both groups, which is similar to our previous study in postmenopausal women consuming 100 g of dried plum for 1 year[6] demonstrating a slowdown in bone turnover overall. A recent study suggests that bone biomarkers are used by clinicians in making decisions on patient treatment,[17] with concentrations of CTX and P1NP indicated as key biomarkers by the International Osteoporosis Foundation and International Federation of Clinical Chemistry and Laboratory Medicine (IOF–IFCC) Bone Markers Working Group.[17] Although no change in P1NP was detected in our study, the decrease in CTX by dried plum consumption may reflect a clinically meaningful effect and may be a marker for the observed changes in bone morphometry that we detected.

There were no changes observed for total body, spine (L1–L4), dual hip, and ulna BMD as assessed via DXA

Table 3. Daily Physical Activity Calculated from a 7-Day Physical Activity Questionnaire at Baseline, 3, 6, and 12 Months

	Control group				*Dried plum group*			
Variable	*Baseline*	*3 Months*	*6 Months*	*12 Months*	*Baseline*	*3 Months*	*6 Months*	*12 Months*
Sleep (h)	7.3 ± 0.9	7.1 ± 0.9	6.9 ± 1.1	7.0 ± 0.9	7.0 ± 1.0	7.4 ± 1.2	7.2 ± 0.9	6.9 ± 1.1
Physical activity								
Light (h)	13.9 ± 4.1	14.3 ± 3.8	14.7 ± 2.8	15.0 ± 2.2	15.3 ± 1.7	14.9 ± 2.0	15.4 ± 1.4	14.2 ± 4.2
Moderate (h)	1.9 ± 2.4	1.6 ± 1.9	1.5 ± 1.6	1.2 ± 1.5	1.2 ± 1.5	1.2 ± 1.4	1.0 ± 0.8	2.1 ± 3.3
Hard (h)	0.6 ± 1.8	0.7 ± 1.8	0.6 ± 1.2	0.5 ± 0.8	0.5 ± 0.8	0.4 ± 0.7	0.4 ± 0.7	0.6 ± 1.3
Very hard (h)	0.3 ± 1.1	0.3 ± 1.2	0.2 ± 1.2	0.2 ± 0.5	0.1 ± 0.2	0.1 ± 0.4	0.1 ± 1.2	0.1 ± 0.1
kcal/day	3584 ± 1286	3841 ± 1463	3535 ± 1047	3503 ± 909	3371 ± 685	3101 ± 1074	3359 ± 603	3542 ± 985

Data are presented as mean ± SD. Control group: calcium and vitamin D supplement; dried plum group: calcium and vitamin D supplement and 100 g/day dried plum. The Five-City Project Physical Activity recall was used to assess current PA, sleep, and activity pattern including leisure, occupation, and home activities. There were no statistically significant differences observed between the baseline values of the two groups and between baseline, 3, 6, and 12 months corresponding values.

Table 4. Effect of 0 and 100 g Dried Plum on Bone Biomarkers

	Control group				*Dried plum group*				P
Biomarker	*Baseline*	*3 Months*	*6 Months*	*12 Months*	*Baseline*	*3 Months*	*6 Months*	*12 Months*	*Time × group*
BAP (U/L)	$22.62^{a} \pm 1.02$	$22.06^{a} \pm 0.96$	$19.82^{b} \pm 0.98$	$16.94^{c} \pm 0.98$	$23.25^{a} \pm 1.33$	$23.77^{a} \pm 1.61$	$20.96^{a,b} \pm 1.8$	$17.33^{b} \pm 0.94$	.001
TRAP5b (U/L)	3.04 ± 0.21	2.71 ± 0.15	2.77 ± 0.19	2.64 ± 0.2	$2.96^{a} \pm 0.18$	$2.72^{b} \pm 0.22$	$2.70^{b} \pm 0.19$	$2.43^{c} \pm 0.18$	.007
CTX (ng/mL)	0.30 ± 0.18	0.28 ± 0.18	0.27 ± 0.17	0.27 ± 0.15	$0.30^{a} \pm 0.16$	$0.27^{b} \pm 0.16$	$0.25^{b} \pm 0.20$	$0.27^{b} \pm 0.15$	NS
P1NP (ng/mL)	48.59 ± 3.28	47.17 ± 2.74	45.00 ± 2.70	46.91 ± 2.88	45.50 ± 3.00	47.41 ± 3.5	43.97 ± 2.97	48.87 ± 4.27	NS
Vitamin D (ng/mL)	47.61 ± 3.54	—	—	48.85 ± 4.27	42.40 ± 2.74	—	—	39.76 ± 2.43	NS

Data are presented as mean ± SE. Control group: calcium and vitamin D supplement; dried plum group: calcium and Vitamin D supplement and 100 g/day dried plum. Means with different superscript letters are significantly different within group, $P < .05$. Baseline values are not different among the two groups.

BAP, bone-specific alkaline phosphatase; CTX, C-terminal collagen cross-links; NS, not significant; P1NP, N-terminal propeptide of type 1 procollagen; SE, standard error; TRAP5b, tartrate-resistant acid phosphatase-5b.

Table 5. Effect of 0 and 100 g Dried Plum on the Bone Mineral Density of the Total Body, Lumbar Spine, Dual Hip, and Ulna Measured by Dual-Energy X-Ray Absorptiometry and on the Left Tibia at 4%, 38%, and 66% Assessed by the Peripheral Quantitative Computed Tomography

	Control group			*Dried plum group*			P		
Variable	*Baseline*	*6 Months*	*12 Months*	*Baseline*	*6 Months*	*12 Months*	*Time*	*Group*	*Time × group*
DXA									
Total body BMD (g/cm^2)	1.29 ± 0.02	1.28 ± 0.02	1.28 ± 0.02	1.28 ± 0.02	1.28 ± 0.02	1.28 ± 0.02	.66	1.00	.76
Lumbar spine (L1–L4) BMD (g/cm^2)	1.27 ± 0.04	1.27 ± 0.04	1.25 ± 0.04	1.28 ± 0.04	1.28 ± 0.04	1.28 ± 0.04	.33	.82	.14
Right hip BMD (g/cm^2)	1.00 ± 0.03	1.00 ± 0.03	1.00 ± 0.03	1.03 ± 0.03	1.03 ± 0.03	1.03 ± 0.03	.91	.37	.78
Left hip BMD (g/cm^2)	1.05 ± 0.04	1.06 ± 0.04	1.06 ± 0.04	1.06 ± 0.03	1.06 ± 0.03	1.05 ± 0.03	.53	.94	.72
Ulna BMD (g/cm^2)	0.72 ± 0.02	0.72 ± 0.02	0.71 ± 0.02	0.71 ± 0.02	0.72 ± 0.02	0.72 ± 0.02	.80	.94	.62
pQCT									
4% Tibia									
Total area (mm^2)	$1336^{*} \pm 42$	1380 ± 38	1377 ± 49	1188 ± 48	1262 ± 34	1255 ± 50	.07	.02	.80
Total density (mg/cm^3)	331 ± 10	330 ± 10	329 ± 12	338 ± 8	339 ± 9	333 ± 10	.97	.62	.92
Trabecular area (mm^2)	$1080^{*} \pm 39$	1113 ± 36	1113 ± 45	939 ± 42	1003 ± 30	1007 ± 44	.12	.02	.72
Trabecular density (mg/cm^3)	284 ± 10	285 ± 9	283 ± 12	279 ± 9	280 ± 9	281 ± 11	.95	.78	.98
BSI (mg^2/mm^4)	147 ± 9	154 ± 11	151 ± 12	136 ± 8	147 ± 9	136 ± 6	.19	.39	.84
38% Tibia									
Cortical density (mg/cm^3)	1153 ± 9	1109 ± 41	1155 ± 13	1162 ± 10	1159 ± 11	1167 ± 4	.28	.21	.43
Cortical content (mg/mm)	400 ± 14	388 ± 20	392 ± 18	399 ± 13	411 ± 15	419 ± 13	.63	.72	.13
Cortical area (mm^2)	345 ± 11	335 ± 17	337 ± 15	341 ± 11	352 ± 11	359 ± 10	.68	.80	.18
Cortical thickness (mm)	5.8 ± 0.2	5.7 ± 0.3	5.7 ± 0.3	6.0 ± 0.2	6.1 ± 0.2	6.3 ± 0.1	.59	.32	.22
Total density (mg/cm^3)	878 ± 19	870 ± 21	869 ± 26	916 ± 13	920 ± 14	929 ± 8	.66	.10	.13
Total content (mg/mm)	424 ± 11	413 ± 18	424 ± 13	422 ± 11	434 ± 12	439 ± 12	.51	.76	.17
Total area (mm^2)	485 ± 10	477 ± 21	496 ± 22	460 ± 10	472 ± 11	472 ± 13	.44	.23	.26
SSI (mm^3)	2286 ± 70	2242 ± 105	2264 ± 92	2201 ± 78	2228 ± 78	2220 ± 94	.50	.46	.37
Periosteal circumference (mm)	77 ± 0.8	76.1 ± 2.7	78 ± 1.6	75 ± 0.9	76 ± 0.9	76 ± 1.0	.52	.44	.35
Endosteal circumference (mm)	41 ± 1.4	40 ± 2.3	42 ± 2.8	38 ± 1.0	38 ± 1.2	37 ± 0.8	.45	.14	.32
66% Tibia									
Cortical density (mg/cm^3)	1105 ± 7.3	1102 ± 8.8	1112 ± 8.8	1099 ± 10.5	1099 ± 10.4	1118 ± 5.1	.19	.86	.63
Cortical content (mg/mm)	415 ± 14	411 ± 15	415 ± 18	392 ± 14	392 ± 16	418 ± 11	.038	.37	.38
Cortical area (mm^2)	374 ± 12	371 ± 13	372 ± 15	353 ± 11	354 ± 12	374 ± 10	.049	.32	.31
Cortical thickness (mm)	4.7 ± 0.2	4.7 ± 0.2	4.7 ± 0.2	4.5 ± 0.1^{b}	4.5 ± 0.1^{b}	4.8 ± 0.1^{a}	.08	.38	.45
Total density (mg/cm^3)	664 ± 17	672 ± 19	665 ± 22	648 ± 13^{b}	$660 \pm 13^{a,b}$	675 ± 14^{a}	.40	.73	.057
Total content (mg/mm)	471 ± 12	470 ± 13	475 ± 15	443 ± 13	448 ± 13	467 ± 12	.049	.21	.14
Total area (mm^2)	720 ± 21	709 ± 24	729 ± 31	676 ± 21	695 ± 21	697 ± 20	.69	.28	.02
SSI (mm^3)	3392 ± 116	3356 ± 129	3412 ± 156	3281 ± 106	3343 ± 121	3377 ± 130	.45	.55	.14
Periosteal circumference (mm)	94.8 ± 1.3	94.0 ± 1.5	95.3 ± 1.9	91.8 ± 1.5	93.2 ± 1.5	93.4 ± 1.4	.71	.28	.02
Endosteal circumference (mm)	64.9 ± 1.9	64.0 ± 2.2	65.7 ± 2.8	63.1 ± 1.5^{b}	$63.3 \pm 1.5^{a,b}$	65.0 ± 1.6^{a}	.74	.70	.02

Data are presented as mean ± SE. Control group: calcium and vitamin D supplement; dried plum group: calcium and vitamin D supplement and 100 g/day dried plum. Means with the asterisk (*) are significantly different between the groups, $P < .05$. Means with different superscript letters are significantly different within group, $P < .05$.

BMD, bone mineral density; BSI, bone strength index; DXA, dual-energy X-ray absorptiometry; pQCT, peripheral quantitative computed tomography; SSI, stress–strain index.

measurements in the control or dried plum groups from baseline to either 6 or 12 months. Modest beneficial effects of dried plums were observed for some changes in bone geometry at 66% region of tibia as detected by pQCT including a tendency ($P = .057$) for BMD to increase in the dried plum group as well as increases in periosteal and endosteal circumferences at 66% region of tibia, which may promote greater bone strength through altered bone remodeling. Although daily consumption of dried plums (50 or 100 g) for 6 and 12 months prevented bone loss in postmenopausal women in previous studies by changing BMD,[6,7] those studies were conducted in osteopenic postmenopausal women. Notably, while some men began the current study with T-scores in the osteopenic and osteoporotic range, the majority of the participants had normal BMD T-scores, which may have limited the likelihood of observing stronger effects.

In comparing responses in male versus female mammals, dried plums may have a more robust effect in female human; however, similar effects among sexes have been demonstrated in animal models.[10–12,14] Interestingly, female ovariectomized mice responded more favorably to consumption of Montgomery blueberries than male mice.[18] Future research is needed to more conclusively examine differences in sex responses to potentially bone building fruits.

Some data suggest that in animals, dried plums may exert some of their bone-protective effects by promoting dose-dependent increases in systemic and local indices of bone formation, for example, serum and mRNA levels of alkaline phosphatase .[10–12,16] In humans, the data are less clear; however, this study and others as recently reviewed[19] suggest that dried plums may limit bone resorption, which could translate to improved structural properties of bone.

The addition of dried plums to the diet contributes $\sim$240 kcal for 100 g doses.[6] Our study participants were advised to maintain their usual diet and physical activity patterns throughout the duration of the study. We did not observe significant changes in energy intake nor in body weight, however, suggesting that the participants compensated for the energy provided by the dried plums.[20] Since self-reported dietary intake and physical activity are known to have limitations and measurement error, it is difficult, however, to draw solid conclusions regarding potential alterations in their diet or physical activity.

Overall, based on the results of bone resorption markers and the pQCT data, the current study suggests that long-term daily consumption of 100 g dried plum exerts modest bone-protective effects in men. Although in the past we have speculatively extrapolated findings from previous studies to men, this clinical study confirms potential modest bone-protective effects of dried plum in men. More studies with larger sample sizes and of osteopenic populations are needed to confirm the findings of this study.

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No competing financial interests exist.

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REFERENCES

1. Penoni D, Fidalgo T, Torres S, *et al.*: Bone density and clinical periodontal attachment in postmenopausal women: A systematic review and meta-analysis. *J Dent Res* 2017;96:261–269.
2. Wright NC, Looker AC, Saag KG, *et al.*: The recent prevalence of osteoporosis and low bone mass in the United States based on bone mineral density at the femoral neck or lumbar spine. *J Bone Miner Res* 2014;29:2520–2526.
3. Adler RA. Osteoporosis in Men. [Updated 2020 May 31]. In: Endotext [Internet] (Feingold KR, Anawalt B, Boyce A, *et al.*, eds) South Dartmouth (MA): MDText.com, Inc., 2000. Available from: https://www.ncbi.nlm.nih.gov/books/NBK558007/.
4. Lambert J, Zaidi M, Mechanick J: Male osteoporosis: Epidemiology and the pathogenesis of aging bones. *Curr Osteoporos Rep* 2011;9:229–236.
5. Hiligsmann M, Cornelissen D, Vrijens B, *et al.*: Determinants, consequences and potential solutions to poor adherence to anti-osteoporosis treatment: Results of an expert group meeting organized by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and the International Osteoporosis Foundation (IOF). *Osteoporos Int* 2019;30:2155–2165.
6. Hooshmand S, Chai S, Saadat R, Payton M, Brummel-Smith K, Arjmandi B: Comparative effects of dried plum and dried apple on bone in postmenopausal women. *Br J Nutr* 2011;106:923–930.
7. Hooshmand S, Kern M, Metti D, *et al.*: The effect of two doses of dried plum on bone density and bone biomarkers in osteopenic postmenopausal women: A randomized, controlled trial. *Osteoporos Int* 2016;27:2271–2279.
8. Hooshmand S, Brisco J, Arjmandi B: The effect of dried plum on serum levels of receptor activator of NF-κB ligand, osteoprotegerin and sclerostin in osteopenic postmenopausal women: A randomised controlled trial. *Br J Nutr* 2014;112:55–60.
9. Arjmandi BH, Lucas EA, Juma S, *et al.*: Dried plums prevent ovariectomy-induced bone loss in rats. *JANA* 2001;4:50–56.
10. Deyhim F, Stoecker BJ, Brusewitz GH, Devareddy L, Arjmandi BH: Dried plum reverses bone loss in an osteopenic rat model of osteoporosis. *Menopause* 2005;12:755–762.
11. Bu S, Lucas E, Franklin M, *et al.*: Comparison of dried plum supplementation and intermittent PTH in restoring bone in osteopenic orchidectomized rats. *Osteoporos Int* 2007;18:931–942.

12. Franklin M, Bu S, Lerner M, *et al.*: Dried plum prevents bone loss in a male osteoporosis model via IGF-I and the RANK pathway. *Bone* 2006;39:1331–1342.
13. Arjmandi B, Khalil D, Lucas E, *et al.*: Dried plums improve indices of bone formation in postmenopausal women. *J Womens Health Gend Based Med* 2002;11:61–68.
14. Halloran BP, Wronski TJ, VonHerzen DC, *et al.*: Dietary dried plum increases bone mass in adult and aged male mice. *J Nutr* 2010;140:1781–1787.
15. Sallis J, Haskell W, Wood P, *et al.*: Physical activity assessment methodology in the Five-City Project. *Am J Epidemiol* 1985;121: 91–106.
16. Rendina E, Hembree K, Davis M, *et al.*: Dried plum's unique capacity to reverse bone loss and alter bone metabolism in postmenopausal osteoporosis model. *PLoS One* 2013;8: e60569.
17. Lane NE, Saag K, O'Neill TJ, *et al.*: Real-world bone turnover marker use: Impact on treatment decisions and fracture. *Osteoporos Int* 2021;32:831–840.
18. Sato AY, Pellegrini GG, Cregor M, *et al.*: Skeletal protection and promotion of microbiome diversity by dietary boosting of the endogenous antioxidant response. *J Bone Miner Res* 2021;36:768–778.
19. Arjmandi BH, Johnson SA, Pourafshar S, *et al.*:: Bone-protective effects of dried plum in postmenopausal women: Efficacy and possible mechanisms. *Nutrients* 2017;9:496.
20. Furchner-Evanson A, Petrisko Y, Howarth L, Nemoseck T, Kern M: Type of snack influences satiety responses in adult women. *Appetite* 2010;54:564–569.