California Prunes

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Prunes. For life.

DIGESTIVE HEALTH

Prunes are the only natural, whole fruit to achieve an authorised health claim in Europe: **Prunes contribute to normal bowel function when 100g are eaten daily**. The EU register 'condition of use of the claim' states: *The claim may be used only for food which provides a daily intake of 100g of dried plums (prunes). In order to bear the claim, information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 100g of dried plums (prunes).* References outlined below include those papers used to support this health claim.

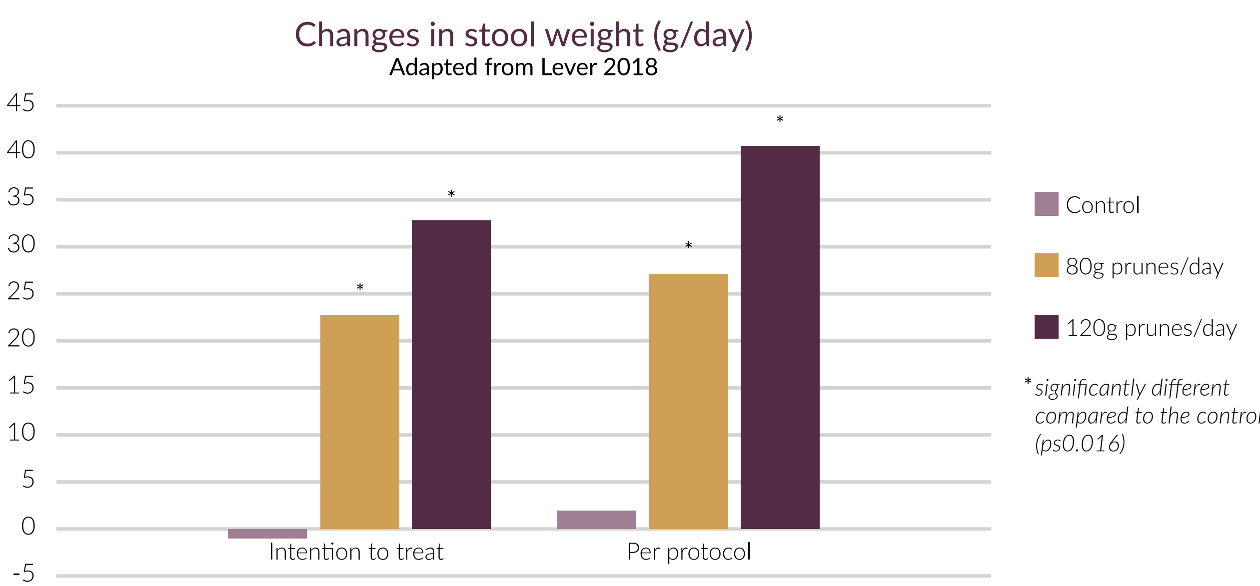
Research carried out by Professor Kevin Whelan's team at King's College London demonstrates encouraging results to further **enhance** the existing EU authorised health claim for prunes and normal bowel function, and clearly demonstrating the efficacy of eating prunes at a **lower consumption rate of 80g**, as opposed to the higher amount of 100g recorded in previous studies (Lever 2018). Eating fewer prunes to achieve the same desired effect may appeal to those who were concerned at the requirement to eat 100g of prunes daily.

The results are also a reminder that encouraging a balanced diet with sufficient fibre, including prunes, represents an efficacious, cost effective and more natural solution to reducing the reliance on over-the-counter (laxative) medication.

120 healthy adults (72% females) with low fibre intakes (15g/d) and infrequent bowel movements (3-6 stools/week) were randomly assigned to one of three groups for 4 weeks: 300ml water (the control group); 80g prunes and 300ml water; or 120g prunes and 300ml water, whilst consuming their regular diet and maintaining normal activity levels. The test food/drink was gradually introduced to reach required levels at day 7, slowly increasing individuals' tolerance to fibre. 91 (76%) people fully complied with the study.

Stool weight and stool frequency significantly increased in those consuming both 80g or 120g prunes (approximately 7-14 prunes), compared to the group only adding water to their daily diet. Transit time was not altered during the study.

Low stool weight and delayed transit time are risk factors for diseases such as colorectal cancer,



haemorrhoids: constipation and increasing fibre intake is the recommended route to reduce the risk of developing these problems. Stool weight is relatively low in developed countries, and it is recommended that this can be addressed by increasing fibre intakes. Fibre intake increased by 29% and 44% in the 80g and 120g prunes groups respectively. Body weight did not significantly change over the 4 weeks of adding prunes to the diet. This reinforces other research that indicates daily consumption of prunes does not detrimentally affect weight.

Bifidobacteria levels significantly increased throughout the study in those consuming prunes. Bifidobacteria is a potentially health-enhancing bacteria that prebiotics are designed to increase.

Furthermore, the researchers noted that the increase was in the same order of magnitude as that observed in some studies investigating the prebiotic effects of inulin and fructo-oligosaccharides and so recommended that more research is warranted to explore the significance of California Prunes microbiota influence.

Further randomised controlled studies exploring the role of prunes in digestive health include Attaluri *et al* (2011) who compared the effects of prunes (50g twice daily) with psyllium (11g twice daily), both containing 6g fibre per day, on common symptoms of constipation for 3 weeks with a 1 week wash out period. This cross over study of 40 subjects with chronic constipation showed that prunes 'were more effective than psyllium for the treatment of mild to moderate constipation and should be considered as a first line therapy'. Other population groups that have been studied include; elderly subjects (Sairanen 2007), post-menopausal women (Shamloufard 2016, Lucas 2004), and men with mild hypercholesterolemia (Tinker 1991).

Potential mechanisms that can explain how prunes may benefit digestive health are suggested to be multifactorial (Stacewicz-Sapuntzakis 2013; Lever 2018; Lever 2014). Additional studies have investigated mechanisms and these include animal studies, which are starting to explore effects on the gut microbiome, and specific disease states such as colon cancer and IBS. Publications in the FASEB Journal (Federation of American Societies for Experimental Biology) offer some preliminary insights into the possible mechanisms of how prunes affect gut health: Seidel (2017) used a rat model of colon carcinogenesis which supports the role of prunes positively, both directly and indirectly, in improving the colon luminal metabolome. Washburn (2017) measured cytokine production in epithelial cells following the addition of polyphenols from prunes and results indicate that prune polyphenols can work to down regulate IL-6 in the gut.

Shamloufard (2016) investigated the bowel function of 48 post-menopausal women who were randomly assigned to consume 0g, 50g or 100g prunes daily for 6 months; diets were also supplemented with 500mg calcium, which is known to increase constipation in post-menopausal women (Reid 2006) and 400 IU vitamin D. Bowel habits were assessed using a 7-day bowel movement questionnaire at baseline, 3 months and 6 months. Constipation ratings were higher in the control group compared to those consuming 100g/day prunes; and consuming 50g or 100g prunes/day 'did not produce adverse effect and may decrease discomfort from bowel movements.'

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SATIETY

Fruit is generally regarded as satiating due to its lower energy content compared to other foods, and its fibre content. The form of the fruit may impact satiety; fruit juice for example has a lower fibre content than its fresh fruit equivalent, and research has suggested that juice has a lower satiating effect than the whole fruit (Farajian 2010). Dried fruit is more energy dense due to the removal of water (energy and fibre content per individual fruit is similar however), and tends to be a source of fibre, so its effect on satiety may also differ.

Prunes have a low GI of 29 (Foster-Powell 2002) and high fibre content (7.1g/100g), and their role in satiety has been explored in several human studies, including by the research team at Liverpool University (Harrold *et al* 2014), who investigated the effect of high dose prune intake (140-171g/day) in 100 overweight and obese adults as part of a weight management programme. This randomised between-subjects study assessed the effects of prunes on weight and appetite in comparison to an active control (advice on healthy snacks) over a 12-week period of active weight loss. The results demonstrated that consuming large quantities of prunes daily did not result in detrimental effects on body weight; in fact subjects consuming prunes as part of a healthy life-style intervention produced significant changes in body weight (1.99kg/2.4%; $p<0.000$) and waist circumference (2.5cm/2.3%; $p<0.000$) from baseline, with results at least as good as those subjects consuming the healthy snacks. Furthermore those in the prune group had a trend for greater weight loss (p=0.07) in the last 4 weeks of the study and, despite the high daily doses, the prunes were well tolerated, giving some indication of prunes' potential to contribute to long term weight management. The researchers propose that this may relate to chronic appetite effects since area under the curve (AUC) analysis demonstrated increased fullness in the prune group after week 8 (p=0.05).

Lever (2018) also showed that body weight did not significantly change following the addition of 80g or 120g prunes daily to the regular diet of 120 healthy adults for 4 weeks who maintained normal activity levels. Furchner-Evansons (2010) compared the effects of snacks - prunes, low fat cookies, white bread, and water (used as a control) - on satiety in 19 women. The fibre and sugar content of the snacks differed, but were matched for energy (238kcal), with similar carbohydrate, fat and protein content. Snacks were consumed on different days, and separated by at least one day. Satiety was assessed by hunger ratings for 2 hours following the snack, and then subjects consumed a meal until they were satisfied. The authors concluded that 'consuming prunes as a snack suppresses hunger relative to a low-fat cookie as evidenced by lower glucose and/or satiety-regulating hormone concentrations'.

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BONE HEALTH

Research into the role of prunes in bone health, continues to grow, with human, animal and in vitro studies and two recent research reviews (Arjmandi 2017; and Wallace 2017) summarising current knowledge. Although the exact mechanism for the protective effects remains to be confirmed, Arjmandi (2017) concludes: 'it is likely that there are additive and/or synergistic effects among these [bioactive] compounds [in prunes]', and Wallace (2017) concludes that these 'may in part be due to the unique variety of phenolics and nutrients present'.

A randomised controlled trial by Hooshmand *et al* (2016) monitored bone mineral density (BMD) in 48 osteopenic, post-menopausal women aged 65-79, who ate 0g (control), 50g or 100g prunes daily for 6 months. All subjects consumed a calcium and vitamin D supplement daily. Those receiving the supplements with the prunes fared better, showing a significantly higher total body bone mineral density than those who took the supplements with no prunes. This research builds on earlier work (Hooshmand 2011), which randomly assigned 160 post-menopausal women to two groups supplemented with 100g prunes or 75g apples (energy, carbohydrate, fat and fibre levels were similar), alongside calcium and vitamin D supplements daily. Following the year-long study, authors concluded that prunes improved 'bone mass by slowing down the rate of bone turnover'.

Arjmandi (2017) provides follow up results of 20 women from the original 100 in an earlier study. These results suggest that women who consumed 100g prunes a day for a year retained bone density in the lumbar spine and ulna to a greater extent than the control group (dried apples) after 5 years, even though they no longer regularly consumed prunes. Shamloufard (2016) studied the bowel function of a sample of this population group and found that constipation rates were lower in the prune group compared to the control.
(see **digestive health** section for full details)

A randomised cross over trial (Al-Dashti 2019) monitored changes to C-telopeptide, beta cross-linked (CTX), the now recommended reference marker of bone resorption (a predictor of fracture risk) in clinical studies, following short term, modest prune intake. As part of their habitual diet 27 healthy post-menopausal women snacked on 2 or 6 prunes daily (approximately 14g and 42g respectively) for 2 weeks. Following a 2 week washout period, subjects consumed the other study arm. Whilst CTX marker remained unchanged compared to baseline in both groups, results showed a favourable and significant ($p=0.006$) decline in CTX when subjects consumed 6 prunes during the second phase of the study compared to those consuming 2 prunes in the second phase. The authors recommend this is investigated further.

Whilst research continues to explore the mechanisms by which prunes may benefit bone health, and whether it is specific nutrient components in the prunes, or the whole package that is important, we already know that prunes are high in vitamin K and a source of manganese, two nutrients that contribute to the maintenance of normal bones. They are also high in potassium, which contributes to normal muscle function.

Prunes' synergistic effect was explored by Graef 2018 in aging ovariectomised and control rats. The diets of the ovariectomised rats were supplemented for 3 months with: prunes; polyphenols extracted from prunes; vitamin K; potassium citrate; a combination of polyphenols, vitamin K and potassium as present in 25% w/w prunes; or a control. Whole body bone mass density improved in the prune, polyphenol and combination groups compared to the ovariectomised control rats. Results suggest that prunes' polyphenols may account for '60-80% of the anabolic effect of prunes on bone in vivo' and vitamin K and potassium also have further protective roles.

Graef *et al* used similar methods in two separate studies to assess the effect of polyphenols extracted from California Prune powder on osteoblast and osteoclast activity. In each study, 6 prune polyphenols compounds were tested on cell lines to see which polyphenols had the greatest osteogenic potential either to increase osteoblast differentiation and function (2017a) or decrease osteoclast differentiation and activity (2017b), compared to a control. Those polyphenol fractions identified were then used on bone marrow from the long bones of 4 week old mice for 7 days under normal and inflammatory conditions (by the addition of TNF-a) to further test their effects on expression of genes and proteins involved in osteoblast and osteoclast differentiation and mineralization.

Results from these studies suggest that this is '*an initial step in an effort to determine if certain types of polyphenolic compounds in dried plums promote greater osteogenic activity and these findings warrant follow-up utilizing animal models.*' (Graef 2017a); and that *'These results show that certain types of polyphenolic compounds from dried plum down regulate calcium and MAPK signaling, resulting in suppression of Nfatc 7 expression which ultimately decreases osteoclast formation and activity*' (Graef 2017b).

The benefits are further supported by a small cell culture study (Delgado Cuenca 2017), where the serum of 5 healthy women was collected 1 and 2 hours after the consumption of 100g prunes to monitor changes in osteoblast cell activity and gene expression over 3 and 9 days. Results indicate that osteoblast activity and function were increased.

Schreurs *et al* (2016) explores the bone-preserving role of prunes specific to radiation exposure, such as astronauts in space, and those receiving radiation therapy as part of treatment for cancer. Researchers from the Universities of California, Irvine and Texas looked at the effect of various antioxidant or anti-inflammatory interventions (including California Prune powder and a control) on mice that received radiation. Researchers observed that the California Prune powder was the most effective in reducing undesired bone marrow cells' responses to radiation compared to the other interventions. Additionally, they observed that mice on the prune diet did not exhibit decrements (bone volume loss) after exposure to radiation in any of the structural parameters measured. See abstract on the next page for more details.

Another animal study (Shahnazari 2016) also showed improvements in bone health in both young growing and adult mice following two separate experiments: 1): adult mice (6 months old) were fed a diet containing 25% prunes for 1, 2 or 4 weeks; and 2): growing mice (1 and 2 months old) were fed diets containing 5%, 15% or 25% prunes for 4 weeks. The authors converted the 25% diet to be equivalent to a daily intake of 20 prunes in adults and stated that 'consumption of 4 prunes/day may be expected to have beneficial effects on bone in children'.

Prunes have been shown to exert anti-inflammatory properties and suppress TNF in several studies investigating their effects on bone health. Polyphenols, in particular neochlorogenic acid (present at 91.6-133mg/100g prunes) are considered the bio-actives responsible for prunes' anti-inflammatory effects. Mirza 2018 investigated the specific effects of prunes in both an arthritis induced mouse model (using transgenic mice that overexpress TNF); plus a cell study to explore the anti-inflammatory effects of neochlorogenic acid. Overall results indicated that neochlorogenic acid was able to reproduce many of the same effects as prunes and is likely a bioactive compound in prunes responsible for controlling inflammation mediated signaling of osteoclastogenesis. In contrast to the effects of prunes and their bioactive polyphenols on bone resorption, their effects on bone anabolism remain inconclusive. The authors concluded that 'prunes uncouple bone resorption from bone formation' and although based on animal and in vitro research, they suggest that prunes, due to their bioactive polyphenol content, may have a role in the treatment of rheumatoid arthritis (RA).

Khanna 2017 describes the growing wealth of literature around dietary therapy that is suggestive of a positive impact on RA activity, including prunes, although they stress that no dietary intervention has thus far been conclusively proven. The authors conclude that some dietary recommendations, together with low impact aerobic exercise for self-management, may delay early onset of rheumatoid arthritis, due to providing good sources of natural antioxidants and foods with anti-inflammatory effects.

Osteoporosis is a prevalent and debilitating condition with no signs of subsiding. Rising numbers of people consuming nutrient-poor diets coupled with ageing populations and sedentary lifestyles appear to be the main drivers behind the increasing osteoporosis trend. Aside from calcium and vitamin

Schreurs A, Shirazi-Fard Y, Shahnazari M, Alwood J, Truong T, Tahimic C, Limoli C, Turner N, Halloran B, Globus R (2016) Dried plum diet protects from bone loss caused by ionizing radiation. Scientific Reports 6, Article number: 21343. DOI: 10.1038/srep21343.

Bone loss caused by ionizing radiation is a potential health concern for radiotherapy patients, radiation workers and astronauts. In animal studies, exposure to ionizing radiation increases oxidative damage in skeletal tissues, and results in an imbalance in bone remodelling initiated by increased bone-resorbing osteoclasts. Therefore, we evaluated various candidate interventions with antioxidant or anti-inflammatory activities (antioxidant cocktail, dihydrolipoic acid, ibuprofen, dried plum) both for their ability to blunt the expression of resorption-related genes in marrow cells after irradiation with either gamma rays (photons, 2 Gy) or simulated space radiation (protons and heavy ions, 7 Gy) and to prevent bone loss. Dried plum was most effective in reducing the expression of genes related to bone resorption (Nfe2l2, Ran kl, Mcpl, Opg, TNF-a) and also preventing later cancellous bone decrements caused by irradiation with either photons or heavy ions. Thus, dietary supplementation with DP may prevent the skeletal effects of radiation exposures either in space or on Earth.

D, there is growing evidence that wholefoods and other micronutrients have roles to play in primary and potentially secondary osteoporosis prevention. A review of 20 papers (Higgs *et al*, 2017) has concluded that greater efforts are needed to employ preventative strategies which involve dietary and physical activity modifications, if the current situation is to improve. In particular, 'fruit and vegetables are still not being eaten in adequate amounts and yet contain micronutrients and phytochemicals useful for bone remodelling (bone formation and resorption) and essential for reducing inflammation and oxidative stress.'

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DENTAL HEALTH

The World Health Organisation (WHO 2015) and UK government (SACN 2015) recommend that intakes of free sugars are significantly reduced (to not exceed 5% energy - SACN 2015) due to effects on dental caries and total energy intake, with dental disease being the most prevalent non-communicable diseases (NCDs) globally (WHO 2015). Traditional dried fruit (i.e. without added sugar) is not included as a free sugar (PHE 2018), yet dried fruit intake is currently recommended by dental health professionals to be restricted to meal times only.

Sadler *et al* 2019 explores the complexity of the relationship between dried fruit and dental health, outlining the poor evidence base from which current public health messages to limit consumption to mealtimes have been made. This includes assumptions which are difficult to change, such as dried fruits being high in sugar and therefore damaging to teeth, yet per individual fruit they contain similar amounts of sugar as fresh fruit. Furthermore, little is known about changes to fruit cells during the drying process or how sugar is released from cells during chewing and whether this impacts teeth. Gaps in the evidence need to be investigated further to 'ensure that advice on dried fruit and dental health is truly evidence-based.'

A Review by Sadler published in the International Journal of Food Sciences and Nutrition (2016), with a follow up in Nutrition Bulletin (2017), explores the research around the role of dried fruit, including prunes, and dental health, and the scientific grounds from which the recommendations have been based. Oral health is a complex issue and this literature review shows a lack of consistent data such that more research is needed to ensure evidence-based practice. Sadler (2017) concludes that '*more robust research with validated methods is needed before firm conclusions can be drawn about the retention of dried fruit, and hence its potential for adverse effects on teeth*.'

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OTHER PRUNE RESEARCH AND REVIEWS

The evidence on dried fruit and its role in a healthy diet was reviewed by scientists during an informative healthcare professional workshop in June 2018 and proceedings were published in the International Journal of Food Sciences and Nutrition (Sadler 2019). The workshop was funded by a collaboration between the National Dried Fruit Trade Association, the California Prune Board, the Raisin Administrative Committee, Whitworths and Sunmaid Raisins. Traditional dried fruits contain only naturally occurring sugars with no added sugars or free sugars and are nutritionally similar to fresh fruit though more concentrated, with the exception of vitamin C. Topics discussed include the complexity of the relationship between dried fruit and dental health; the public health importance of the gut, which includes prunes' role supporting normal bowel function; satiety; polyphenols; and the nutritional composition of dried fruit. During the round table discussion, it was agreed that there were multiple gaps in the research around many aspects of dried fruit and public health, including its role in dental and gut health, and further research recommendations were proposed. It was also agreed that dried fruit can usefully contribute to the 30g/day fibre and 5-A-Day fruit and vegetable recommendations, so important for optimal health and currently difficult to achieve.

The nutrient composition of foods, including prunes, can vary due to multiple factors including country of origin, harvesting, crop variations, processing methods, storage conditions and soil management. Professor Kevin Whelan's team at King's College London have reported the compositional analysis of prunes (Gill 2019) from four key prune producing countries (USA (43% of global supply), Chile (24%), France (16%) and Argentina (15%)), by purchasing samples from retailers across five major European markets (France, UK, Italy, Spain and Germany). The researchers also specifically compared the compositional data for American (Californian) prunes against data published in UK and US databases.

The USDA database, unsurprisingly, more accurately reflected the nutrient composition of American (Californian) prunes measured in this study compared to the UK database, in particular for energy and starch. Discrepancies in energy content are in part due to variations in national energy conversion factors: unlike in the UK data excludes fibre and polyols from the energy calculations, whereas this is included for US data.

Gill *et al* recommends existing databases (McCance and Widdowson (UK) and USDA (USA)) are updated: to reflect components relevant to gut health (e.g. different fibre fractions and sorbitol content); to update old data (previously compiled between 1980 and 2001) which may '*no longer accurately reflect present-day prune composition*'; and to consider unavailable carbohydrates in the total carbohydrate calculation (USDA data).

Research exploring the various ways that prunes may benefit health now spans a wide range of both human and animal studies, as well as in

The following review explores the potential health effects of prunes, this updates the original review by Stacewicz-Sapuntzakis published in 2001.

Stacewicz-Sapuntzakis M (2013) Dried Plums and Their Products: Composition and Health Effects - An Updated Review. Critical Reviews in Food Science and Nutrition. 53; 1277-302.
https://doi.org/10.1080/10408398.2011.563880

Abstract

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 KI, 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.

Hooshmand S, Kumar A, Zhang J, Johnson S, Chai S, Arjmandi B (2015) Evidence for anti-inflammatory and antioxidative properties of dried plum polyphenols in macrophage RAW 264.7 cells. Food Funct. 6; 1719-25.

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Abstract

This study presents the anti-inflammatory and antioxidative properties of dried plum (*Prunus domestica L.*) polyphenols in macrophage RAW 264.7 cells. We hypothesized that dried plum polyphenols have strong anti-inflammatory and antioxidant properties against lipopolysaccharide (LPS)-induced production of the proinflammatory markers, nitric oxide (NO) and cyclooxygenase-2 (COX-2), and the lipid peroxidation product, malondialdehyde, in activated macrophage RAW 264.7 cells.

To test this hypothesis, macrophage RAW 264.7 cells were stimulated with either 1 µg ml(-1) (for measurement of NO production) or 1 ng ml(-1) (for measurement of COX-2 expression) of LPS to induce inflammation and were treated with different doses of dried plum polyphenols (0.0, 0.1, 1, 10, 100 and 1000 µg ml(-1)). Dried plum polyphenols at a dose of 1000 µg ml(-1) was able to significantly ($P < 0.05$) reduce NO production by 43%. Additionally, LPS-induced expression of COX-2 was significantly ($P < 0.05$) reduced by 100 and 1000 µg ml(-1) dried plum polyphenols. To investigate the antioxidant activity of dried plum polyphenols, macrophage RAW 264.7 cells were stimulated with 100 µg ml(-1) of $FeSO_4$ + 1 mM ml(-1) of H_2O_2 to induce lipid peroxidation. Dried plum polyphenols at a dose of 1000 µg ml(-1) showed a 32% reduction in malondialdehyde production. These findings indicate that dried plum polyphenols are potent anti-inflammatory and antioxidative agents in vitro. DP may prevent the skeletal effects of radiation exposures either in space or on Earth.

vitro research. These include exploratory work on anti-cancer, anti-inflammatory and antioxidant properties, in particular Hooshmand *et al* 2015 tested the anti-inflammatory and anti-oxidative properties of prune polyphenols in macrophage cells, as outlined in the abstract to the left.

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