Healthcare Professionals Newsletter

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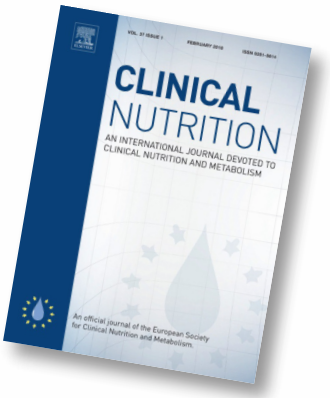
FURTHER PROOF THAT PRUNES SUPPORT BOWEL HEALTH

NEW RESEARCH BY PROFESSOR KEVIN WHELAN OF KING'S COLLEGE LONDON – the renowned centre of excellence for nutrition and digestive health - 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. Eating less 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 and cost effective, more natural solution to reducing the reliance on over-the-counter (laxative) medication. (Lever E, *Clinical Nutrition* 2018).



An independent randomised control trial published in the journal 'Clinical Nutrition' was undertaken by King's College London, UK – the renowned centre of excellence for nutrition and digestive health – with colleagues from Queen Mary University of London and the University of Aberdeen and was funded by the California Prune Board. The findings demonstrate the efficacy of eating prunes at a **lower consumption rate of 80g,** as opposed to the higher amount of 100g recorded in previous studies. Eating less prunes to achieve the same desired effect may appeal to those who were concerned at the requirement to eat 100g of prunes as per the original EFSA health claim.

This controlled trial is the first to take the EU health claim data further by following the **stringent research requirements defined by EFSA** (European Food Safety Authority) and measuring the impact on bowel function **using objective measures** of demonstrated importance to gut health (stool weight, transit time) as opposed to previous studies which relied on self-reporting mechanisms.

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 were gradually introduced to reach required levels at day 7 to slowly increase 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 and 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 observed 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 more research is warranted to explore the significance of California prunes microbiota influence.

The research could also be relevant to helping to address the UK's mounting laxative bill – according to NHS England, the spend on laxatives has increased by 61.2% over the last 10 years! Eating more fibre rich foods such as prunes could potentially reduce the need for such interventions!

References:
Lever E, Scott M, Louis P, Emery P, Whelan K (2018) The effect of prunes on stool output, gut transit time and gastrointestinal microbiota: A randomised controlled trial. *Clinical Nutrition*. Available at: http://www.clinicalnutritionjournal.com/article/S0261-5614(18)30003-7/fulltext?rss=yes

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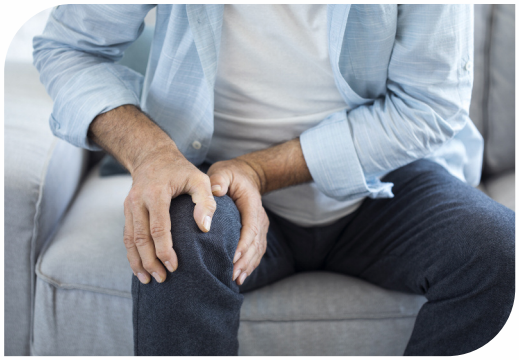
IN THIS ISSUE...

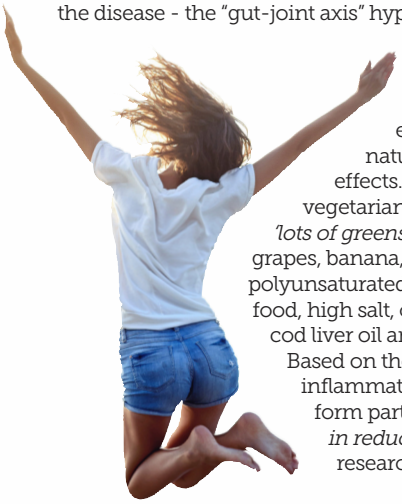
DIET AND RHEUMATOID ARTHRITIS



RHEUMATOID ARTHRITIS (RA) IS A DEBILITATING, CHRONIC INFLAMMATORY AUTOIMMUNE DISORDER, WITH HIGH DRUG COSTS AND A SEVERE IMPACT ON QUALITY OF LIFE FOR SUFFERERS. It results in joint destruction and bone loss and although the exact causes remain unknown, environmental (eg smoking, infectious diseases) and genetic factors are equally responsible. The disease affects approximately 1% of the world population, appears to be more prevalent in women than men (53/100,000 women vs 28/100,000 men), and causes higher mortality, work disability and decreased functional capacity compared to those without RA of the same age.

This burden of increased morbidity and mortality in RA sufferers, together with the high drug treatment costs, provided the rationale for a recent literature review, (Khanna S, *Front Nutr* 2017;4:52) explores different dietary approaches to treating RA, including prunes. Khanna et al (2017) describe the growing wealth of literature around dietary therapy that is suggestive of a positive impact on RA activity, although they stress that no dietary intervention has thus far been conclusively proven. Nevertheless, reducing symptoms through diet, within an overall healthy dietary pattern is a sensible approach, since drugs currently in use are also not 100% effective.

Addressing diet is made more relevant by the increasing understanding of microbiota mediated disease pathology and the beneficial effects of nutrients on inflammation and immunity. RA sufferers often complain of gastrointestinal symptoms as well as painful joints, which has stimulated suggestions that the gut microbiota may be involved with the disease - the "gut-joint axis" hypothesis.



The authors conclude with some dietary recommendations together with low impact aerobic exercise for self-management of RA that may delay early onset of RA, due to providing good sources of natural antioxidants and foods with anti-inflammatory effects. They promote the benefits of eating more vegetarian/vegan diets, raw or moderately cooked vegetables *'lots of greens, legumes',* fruits, including prunes, grapefruits, grapes, banana, apples; probiotic yogurt; turmeric and ginger; polyunsaturated fatty acid/ oleic acid; and avoiding any processed food, high salt, oils, butter, sugar, and animal products. Vitamin D, cod liver oil and multivitamins supplements are also suggested. Based on the review, the authors have designed an anti-inflammatory food chart, which focuses on wholefoods that form part of a healthy balanced diet – these foods *'may aid in reducing signs and symptoms of RA',* although more research is needed to confirm a role for all these foods.

Recommended anti-inflammatory food chart (Khanna 2017):

Fruits	Dried plums, grapefruits, grapes, blueberries, pomegranate, mango (seasonal fruit), banana, peaches, apples
Cereals	Whole oatmeal, whole wheat bread, whole flattened rice
Legumes	Black soybean, black gram
Whole grains	Wheat, rice, oats, corn, rye, barley, millets, sorghum, canary seed
Spices	Ginger, turmeric
Herbs	Sallaki, ashwagandha
Oils	Olive oil, fish oil, borage seed oil (in incapsulated form)
Miscellaneous	Yogurt (curd), green tea, basil (tulsi) tea

Prune it for kids

With childhood obesity[1] and dental decay on the rise due in part to excessive sugar intake amongst UK children, California prunes offer a high fibre, convenience fruit that can effectively reduce the added sugar and fat in children's food. Their unique blend of pectin and sorbitol offers fat-like (though fat-free) characteristics that enhance flavour and shelf-life. 100kcal California prunes provides 3.1g fibre (44g portion).

These delicious prune cookies contain 51 kcal per cookie.

http://www.californiaprunes.co.uk/recipe/quick-california-prune-cookies/

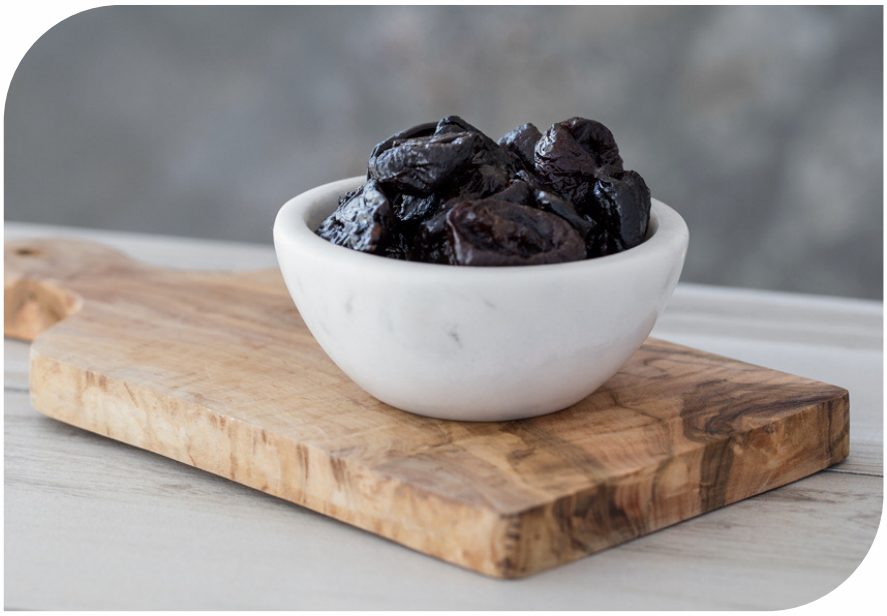
(1) Nearly a third of children aged 2-15 years are overweight or obese, and children are becoming obese earlier and staying obese for longer. Source: HM Government (2016) Childhood Obesity: A Plan for Action. Available at: https://www.gov.uk/government/publications/childhood-obesity-a-plan-for-action [Accessed 23/01/2017].

PRUNES FROM CALIFORNIA®

RHEUMATOID ARTHRITIS: A SPECIFIC ROLE FOR PRUNES?

ONE OF THE FACTORS CONTRIBUTING TO RA PROGRESSION is the production of inflammatory mediators including tumour necrosis factor (TNF), the net result being the formation of synovitis and the destruction of bone and cartilage. Drug therapy for RA includes anti-TNF-therapies which are costly, produce unfavourable immunosuppressive properties and have an increased risk of infectious diseases.

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 bioactives responsible for prunes anti-inflammatory effects. A new study adds to this body of evidence. Mirza F et al (*J Nutr Bioc* 2018;54;54-61) 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.



Inflammation-induced joint bone damage was measured in female transgenic mice fed either a regular growth diet or a diet containing 20% California Prunes. A third group of similar aged female non-transgenic mice were fed the regular growth diet and served as a negative control. 2.2g of diet were consumed daily for 4 weeks and each diet had comparable calories, macronutrients and sugar.

As expected transgenic mice on the regular diet exhibited bone destruction, whereas supplementation with prunes resulted in a significant recovery of bone mass at the knee and the fourth finger proximal interphalangeal joint. This suggests that the prune diet reduced osteoclast activity (bone breaking cells), so preserving bone mass.

The researchers then tested the anti-inflammatory effects of neochlorogenic acid on human synovial fibroblasts in the lab, by measuring the effect of TNF with or without neochlorogenic acid. The addition of neochlorogenic acid resulted in lower expressions of TNF induced inflammatory markers. Osteoblasts, the bone forming cells also contribute to management of bone mass, but when the effect of neochlorogenic acid on osteoblasts that were treated with TNF was measured, it did not affect osteoblast differentiation.

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 signalling of osteoclastogenesis.

In contrast to the effects of prunes and its 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 RA.

While we wait for more high quality, human studies into the role of diet in RA, these papers reiterate that a healthy, wholefood diet is a good insurance policy. Specifically, prunes may offer a triple bonus of 'proven' gut health, plus 'well researched' bone health and now 'plausible' benefit in rheumatoid arthritis.

References:

Khanna S, Jaiswal KS and Gupta B (2017) Managing Rheumatoid Arthritis with Dietary Interventions. Front. *Nutr.* 4:52. DOI: 10.3389/fnut.2017.00052

Mirza F, Lorenzo J, Drissi H, Lee F, Soung D (2018) Dried plum alleviates symptoms of inflammatory arthritis in TNF transgenic mice. *Journal of Nutritional Biochemistry.* 52; 54–61. https://doi.org/10.1016/j.jnutbio.2017.10.002

Prune essence concentrate benefits intestinal function and blood lipids

A randomised control trial (Chiu H, *Pharmaceutical Biology* 2017; 55:974-979) using prune essence concentrate for 4 weeks in 60 healthy mild hypercholesterolemic subjects showed significant improvements to gut microbiota and reductions in total and LDL cholesterol. To review the full paper please visit http://www.tandfonline.com/doi/full/10.1080/13880209.2017.1285323

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FURTHER EVIDENCE FOR THE ROLE ON PRUNES IN BONE HEALTH

ADDING TO THE GROWING NUMBER OF HUMAN AND ANIMAL STUDIES LOOKING AT THE BENEFICIAL ROLE OF PRUNES IN BONE HEALTH, (Graef J. *J Nutr Bioc* 2017; Graef. *Curr Dev Nutr* 2017), carried out in vitro studies to add to our understanding of the mechanism behind the beneficial effects of prunes reported to date. Prunes are high in vitamin K and a source of manganese, which contribute to the maintenance of normal bones.

Graef et al used similar methods in two separate studies to assess the effect of polyphenols extracted from California prune powder on osteoclast and osteoblast 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-α) to further test their effects on expression of genes and proteins involved in osteoblast and osteoclast differentiation and mineralization.

Osteoblast

DP-FrA and DP-FrB polyphenol fractions were identified as having the greatest osteogenic potential and both chlorogenic and cryptochlorogenic acid were detected in these fractions. Isomers of chlorogenic acid have been reported to have antioxidant and anti-inflammatory properties, and to alter cell signalling pathways. Results using these two fractions in primary bone marrow-derived osteoclast culture experiments demonstrated significantly increased ALP activity (an indicator of osteoblast activity) at day 3 of treatment compared to the control, DP-FrB further reduced this at day 7, and both factions significantly increased mineralised nodule formation in bone marrow-derived osteoblasts in normal conditions compared to the control. A trend towards improvements was also seen under inflammatory conditions. Gene expression analysis was also carried out to assess changes in signalling pathways. *Bmp2* mRNA (a gene known to be upregulated with increased bone mineralisation); *Runx2* (transcription factor that activates genes related to osteoblast differentiation); Bsp (promotes mineralisation on osteoblasts); and *Phex* (promotes matrix mineralisation) expressions were increased with the 2 polyphenols fractions, compared to the control, and were normalised 24 hours after treatment. The author concludes that the *"data show that the dried plum polyphenolic fractions can increase bone formation by inducing the gene expression of regulators of differentiation and mineralization activity of osteoblasts."*

This study 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."*

Osteoclasts

3 polyphenol fractions (DP-FrE, DP-FrF and DP-FrA) were identified as reducing osteoclast activity compared to the control under normal and inflammatory conditions in the initial screening part of the study. These results were further confirmed for 2 of the fractions (DP-FrE and DP-FrF) using primary bone marrow-derived cultures where osteoclast differentiation and activity was reduced in normal and inflammatory conditions.

Nfatc1 (which regulates osteoclastogensis) and *Traf6* (involved in osteoclast differentiation) were down regulated in normal and inflammatory conditions with the polyphenol fractions. *Rankl* expression was not altered during normal conditions, but was down regulated under inflammatory conditions.

The role of prune polyphenols in bone health was further measured in an osteoblast and osteoclast interaction model and the results suggest that prune polyphenol fractions directly and indirectly reduce osteoclast differentiation.

The authors concluded that '*These results show that certain types of polyphenolic compounds from dried plum down regulate calcium and MAPK signaling, resulting in suppression of Nfatc1 expression which ultimately decreases osteoclast formation and activity.*'

Prune powder pholyphenols DP-FrE and DP-FrF contain neochlorogenic acid, cryptochlorogenic acid and rutin, with the DP-FrF being the most bioactive and as such merits further differentiation. The authors conclude that further in vivo investigations on these bioactive prune components are now warranted before any therapeutic treatment could be considered.

Osteoporosis - A Crippling Health Problem

- Osteoporosis affects an estimated 75 million people in Europe, USA and Japan.
- 1 in 3 women over 50 will experience osteoporotic fractures, as will 1 in 5 men.
- The combined lifetime risk for hip, forearm and vertebral fractures coming to clinical attention is around 40%, equivalent to the risk for cardiovascular disease.
- Osteoporosis takes a huge personal and economic toll. In Europe, the disability due to osteoporosis is greater than that caused by cancers (with the exception of lung cancer) and is comparable or greater than that lost to a variety of chronic noncommunicable diseases, such as rheumatoid arthritis, asthma and high blood pressure related heart disease.
- In women over 45 years of age, osteoporosis accounts for more days spent in hospital than many other diseases, including diabetes, myocardial infarction and breast cancer.

For more Osteoporosis stats visit International Osteoporosis Foundation (2017) Osteoporosis facts and statistics. To view click here.

References:

a). Graef J, Rendina-Ruedy E, Crockett E, Ouyang P, King J, Cichewicz R, Lucas E, Smith B. Select polyphenolic fractions from dried plum enhance osteoblast activity through BMP-2 signaling. *The Journal of Nutritional Biochemistry* (2017), https://doi.org/10.1016/j.jnutbio.2017.09.014

b. Graef J, Rendina-Ruedy E, Crockett E, Ouyang P, Wu L, King J, Cichewicz R, Lin D, Lucas E, Smith B. Osteoclast Differentiation is Downregulated by Select Polyphenolic Fractions from Dried Plum via Suppression of MAPKs and Nfatc1 in Mouse C57BL/6 Primary Bone Marrow Cells. *Current Developments in Nutrition* (2017), 1;10. https://doi.org/10.3945/cdn.117.000406

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