

Dried plum protects from radiation-induced bone loss by attenuating pro-osteoclastic and oxidative stress responses

R. Globus, et al.

Future space explorations beyond the earth's magnetosphere will increase human exposure to space radiation and associated risks to skeletal health. We hypothesize that oxidative stress resulting from radiation exposure plays a major role in progressive bone loss and dysfunction in associated tissue. In animal studies, increased free radical formation is associated with pathological changes in bone structure, enhanced bone resorption, reduced bone formation and decreased bone mineral density, which can lead to skeletal fragility. Our long-term goals are to define the mechanisms and risk of bone loss in the spaceflight environment and to facilitate the development of effective countermeasures. We had previously reported that exposure to low or high-LET radiation correlates with an acute increase in the expression of pro-osteoclastic and oxidative stress genes in bone during the early response to radiation followed by pathological changes in skeletal structure. We then conducted systematic screening for potential countermeasures against bone loss where we tested the ability of various antioxidants to mitigate the radiation-induced increase in expression of these markers.

For the screen, 16-week old C57Bl6/J mice were treated with a dietary antioxidant cocktail, injectable DHLA or a dried plum-enriched diet (DP). Mice were then exposed to 2Gy ¹³⁷Cs radiation and one day later, marrow cells were collected and the relevant genes analyzed for expression levels. Among the candidate countermeasures tested, DP was most effective in reducing the expression of genes associated with bone loss. Furthermore, analysis of skeletal structure by microcomputed tomography (microCT) revealed that DP also prevents the radiation-induced deterioration in skeletal microarchitecture as indicated by parameters such as percent bone volume (BV/TV), trabecular spacing and trabecular number. We also found that DP has similar protective effects on skeletal structure in a follow-up study using 1 Gy of sequential proton and iron, radiation species relevant to spaceflight. When cultured ex vivo under osteogenic conditions, bone marrow-derived cells from DP-fed animals exhibited increased colony numbers compared to control diet-fed animals. These findings suggest that DP exerts pro-osteogenic effects apart from its previously demonstrated anti-resorptive action, which may be one of the mechanisms underlying its radioprotective effect on bone. In conclusion, a diet enriched in certain types of antioxidants may be useful as an intervention for radiation-induced bone loss.