

Prevention of Bone Loss by Phloridzin, an Apple Polyphenol, in Ovariectomized Rats under Inflammation Conditions

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Abstract. Aging and sex hormones related changes lead to inflammatory and oxidant conditions, which are involved in the pathogenesis of osteoporosis. Recent studies have suggested that polyphenols may exert a protective effect in such conditions. We assessed the effect of phloridzin (Phlo), a flavonoid exclusively found in apple, on bone metabolism in ovariectomized (OVX) or sham-operated (SH) rats with and without inflammation. Six-month-old Wistar rats were allocated to two equal groups that received either a control diet or a diet supplemented with 0.25% Phlo for 80 days. Three weeks before necropsy, inflammation was induced by subcutaneous injection of talc in 10 animals of each group. At necropsy, ovariectomy decreased both total (T-BMD) and metaphyseal (M-BMD) femoral bone mineral density ($P < 0.01$). Inflammation conditions, checked by an increase in the spleen weight and $\alpha 1$ -acid glycoprotein concentration in OVX rats, exacerbated the decrease in T-BMD (g/cm^2) (as well as M-BMD) observed in castrated animals ($P < 0.05$). Daily Phlo intake prevented ovariectomy-induced bone loss in conditions of inflammation as shown by T-BMD and M-BMD ($P < 0.05$). At the diaphyseal site, BMD was improved by Phlo in OVX rats with or without inflammation ($P < 0.05$). These results could be explained by changes in bone remodeling as the increased urinary deoxypyridinoline excretion in OVX and OVX_{inf} animals was prevented by the polyphenol-rich diet ($P < 0.001$), while plasma osteocalcin concentration was similar in all experimental groups. In conclusion, Phlo consumption may provide protection against ovariectomy-induced osteopenia under inflammation conditions by improving inflammation markers and bone resorption.

Key words: Phloridzin — Bone-sparing effect — Ovariectomized rat — Inflammation

With the human race experiencing a progressive increase in life expectancy, osteoporosis has become a major

cause of morbidity, disability, and increased medical care costs in many regions of the world [1].

Basically, this metabolic disease is associated not only with a decline in the secretion of numerous hormones (mainly sex hormones) but also with an impaired inflammatory status. Indeed, estrogen deficiency in postmenopausal women is associated with an increase in local production of various cytokines and growth factors within the bone microenvironment. Ralston et al. [2] demonstrated that interleukin-1 (IL-1), tumor necrosis factor (TNF), and IL-6 mRNAs are expressed more frequently in bone cells from untreated postmenopausal women than from those on estrogen replacement therapy. Those proinflammatory cytokines intervene in osteoclastogenesis by increasing bone resorption, both directly and through the stimulation of other local factors [3].

There is an increasing rationale to focus on early prevention in order to avoid or delay functional impairments [4]. Nutritional strategies for optimizing bone health are extremely important since a dietary approach is more popular among osteoporosis sufferers than drug intervention and long-term drug treatment compliance is relatively poor. Moreover, the low prophylaxis with hormone replacement therapy will be further limited because of concerns over an increased risk of malignancy and cardiovascular diseases [5–8].

Epidemiological studies have shown that consumption of fruits and vegetables is associated with reduced risk of osteoporosis [9]. Actually, vegetable products contain a complex array of naturally occurring bioactive nonnutrients called *phytochemicals* that may confer significant long-term health benefits. Among them, some phenolic compounds may have applications as anti-inflammatory and bone-sparing agents. Horcajada-Molteni and Coxam [10] have shown that rutin, found in high levels in onions, improves bone quality in the ovariectomized (OVX) rat, an animal model for postmenopausal osteoporosis. Moreover, Wattel et al. [11]