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Pomegranate seed oil for nutritional management of postmenopausal osteoporosis: *in vitro* and preclinical studies

Mélanie Spilmont$^{1,2,3,6}$, Laurent Léotoing$^{1,2,3}$, Marie-Jeanne Davicco$^{1,2,3}$, Patrice Lebecque$^{1,2,3}$, Sylvie Mercier$^{1,2,3}$, Elisabeth Miot-Noirault$^{4,5}$, Laurent Rios$^6$, Yohann Wittrant$^{1,2,3}$, Véronique Coxam$^{1,2,3,*}$

$^1$INRA, UMR 1019, UNH, CRNH Auvergne, F-63009 Clermont-Ferrand, France
$^2$Equipe Alimentation, Squelette et Métabolismes
$^3$Clermont Université, Université d’Auvergne, Unité de Nutrition Humaine, BP 10448, F-63000 Clermont-Ferrand, France
$^4$Clermont Université, Université d’Auvergne, Imagerie moléculaire et thérapie vectorisée, BP 10448, F-63000 Clermont-Ferrand, France
$^5$Inserm, U 990, F-63000 Clermont-Ferrand, France
$^6$GREENTECH SA Biopôle Clermont-Limagne 63360 Saint-Beauzire – France

In the current context of longer life expectancy, the prevalence of osteoporosis is increasingly important. This is why development of new strategies of prevention is highly suitable. Some dietary fats and particularly conjugated linoleic acid have a positive impact on bone formation leading to improved bone mineral density (BMD). Pomegranate seed oil (PSO) and its major component: punicic acid, a conjugated linolenic acid specific to this fruit, have potent anti-inflammatory and anti-oxidative properties both *in vitro* and *in vivo*, two process strongly involved in osteoporosis establishment. In this study, we demonstrated that PSO consumption (5% of the diet) improved significantly bone BMD and prevented trabecular microarchitecture impairment in ovariectomized (OVX) mice C57bl6j, compared to OVX controls animals. Those findings are associated with transcriptional changes in bone tissue, suggesting involvement of both osteoclastogenesis inhibition and osteoblastogenesis improvement. In addition, thanks to an *ex-vivo* experiment, we provided evidence that serum from mice fed pomegranate seed oil (5% by gavage) had the ability to significantly down-regulate the expression of specific osteoclast differentiation markers and RANK-RANKL downstream signaling targets in osteoclast like cells (Raw264.7). Moreover, in osteoblast like cells (MC3T3-E1) it elicited significant increase in ALP activity, matrix mineralization and transcriptional levels of major osteoblast lineage markers involving the Wnt/β-catenin signaling pathways may. Our data also reveal that PSO inhibited pro-inflammatory factors expression, while stimulating anti-inflammatory ones. These results demonstrate that PSO is highly relevant regarding osteoporosis. Indeed, it offers promising alternatives in the design of new strategies in nutritional management of age-related bone complications.