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Phosphorylated Peptides from Antarctic Krill (*Euphausia superba*) Ameliorated Osteoporosis by Activation of Osteogenesis-related MAPK and PI3K/AKT/GSK-3 β pathways in dexamethasone-treated

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Glucocorticoid is widely used as an effective therapy for alleviating chronic inflammatory and autoimmune diseases. However, long-term use of glucocorticoids is accompanied by severe side effects, including increased incidence of osteoporosis. In the current study, the effects of phosphorylated peptides from Antarctic krill (PP-AKP) on osteoporosis induced by dexamethasone were investigated in vivo. Results showed that PP-AKP significantly improved bone turnover status, reduced bone loss and degeneration of microarchitecture, in addition to accelerated bone formation. Further mechanism investigation revealed that PP-AKP suppressed the mRNA expression of MKP-1 and CB1, which activated the downstream osteogenesis-related MAPK and PI3K/AKT/GSK-3 β signaling pathways through elevation of the expression of the key factors p38, ERK, PI3K, AKT and β -catenin, in addition to osteogenic nuclear transcription factors Runx2 and OSX. Additionally, reduction in number of adipocytes and an increase in trabeculae in the bone marrow cavity, in addition to a decrease in abdominal adipose further verified that PP-AKP augmented bone formation with a comparable reduction in the accumulation of fat. Our results suggested that PP-AKP might serve as a potential functional ingredient against osteoporosis.