題名:Icariin isolated from Epimedium pubescens regulates osteoblasts anabolism through BMP-2, SMAD4, and Cbfa1 expression.

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摘要:Epimedii herba is one of the most frequently used herbs in formulas prescribed for the treatment of osteoporosis in China. The main active flavonoid glucoside extracted from Epimedium pubescens is Icariin, which has been reported to enhance bone healing and reduce osteoporosis occurrence. However, the detailed molecular mechanisms remain unclear. In this present study, we examine the molecular mechanisms of icariin by using primary osteoblast cell cultures obtained from adult mice. The osteoblast cells were harvested from 8-month old female Imprinting Control Region (ICR) mice. The effects of icariin stimulation on the proliferation, differentiation and maturation of osteoblasts were examined. The production of nitric oxide (NO) and caspase-3 were analyzed, along with the gene expressions of bone morphogenetic protein-2 (BMP-2), SMAD4, Cbfa1/Runx2, OPG, and RANKL. The viability of the osteoblasts reached its maximum at 10(-8)M icariin. At this concentration, icariin increased the proliferation and matrix mineralization of osteoblasts and promoted NO synthesis. With icariin treatment, the BMP-2, SMAD4, Cbfa1/Runx2, and OPG gene expressions were up-regulated; the RANKL gene expression was however down-regulated. Concurrent treatment involving the BMP antagonist (Noggin) or the NOS inhibitor (L-NAME) diminished the

icariin-induced cell proliferation, ALP activity, NO production, as well as the BMP-2, SMAD4, Cbfa1/Runx2, OPG, RANKL gene expressions. In this study, we demonstrate that in vitro icariin is a bone anabolic agent that may exert its osteogenic effects through the induction of BMP-2 and NO synthesis, subsequently regulating Cbfa1/Runx2, OPG, and RANKL gene expressions. This effect may contribute to its action on the induction of osteoblasts proliferation and differentiation, resulting in bone formation.
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The viability of the osteoblasts reached its maximum at 108 M icariin. At this concentration, icariin increased the proliferation and matrix mineralization of osteoblasts and promoted NO synthesis. With icariin treatment, the BMP-2, SMAD4, Cbfa1/Runx2, and OPG gene expressions were up-regulated; the RANKL gene expression was however down-regulated. Concurrent treatment

involving the BMP antagonist (Noggin) or the NOS inhibitor (L-NAME) diminished the icariin-induced cell proliferation, ALP activity, NO production, as well as the BMP-2, SMAD4, Cbfa1/Runx2, OPG, RANKL gene expressions.

In this study, we demonstrate that in vitro icariin is a bone anabolic agent that may exert its osteogenic effects through the induction of BMP-2 and NO synthesis, subsequently regulating Cbfa1/Runx2, OPG, and RANKL gene expressions. This effect may contribute to its action on the induction of osteoblasts proliferation and differentiation, resulting in bone formation.