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Isopropanolic extract of black cohosh stimulates osteoprotegerin production by human osteoblasts.

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Abstract

An isopropanolic extract (iCR) from the rhizomes of Cimicifuga racemosa (black cohosh) is used an alternative in the treatment of menopausal symptoms, and animal studies suggest positive skeletal effects. iCR stimulated osteoblastic OPG protein secretion by 3- to 5-fold as early as 12 h without affecting RANKL expression. The iCR effect, abrogated by the pure estrogen receptor antagonist ICI 182,780, also enhanced ALP activity (4-fold) and osteocalcin expression (3-fold), possibly contributing to the skeletal effects of black cohosh.

INTRODUCTION: Despite its positive effects on the skeleton, estrogen replacement therapy is no longer recommended as first-line therapy for the prevention and treatment of postmenopausal osteoporosis because it increases cardiovascular, thromboembolic, and breast cancer risk. Recently, herbal therapeutics such as an isopropanolic extract (iCR) from the rhizomes of Cimicifuga (=Actaea) racemosa (black cohosh) are gaining interest as an alternative in the treatment of menopausal symptoms. Whereas animal studies in rats suggest positive skeletal effects, the mechanism of its actions on bone cells remain unclear. RANKL is essential for osteoclast formation and activation, while osteoprotegerin (OPG) neutralizes RANKL.

MATERIALS AND METHODS: In this study, we assessed the effects of iCR on OPG and RANKL mRNA steady-state levels by semiquantitative RT-PCR and on protein production by an ELISA system in human osteoblasts (hOBs).

RESULTS: Under serum-free conditions, treatment with iCR increased OPG mRNA levels and protein secretion of hOBs by 2- to 3-fold in a dose-dependent manner, with a maximum effect at a 10(6)-fold dilution of iCR ($p < 0.001$) after 24-48 h. Time-course experiments indicated a stimulatory effect of iCR on osteoblastic OPG protein secretion by 3- to 5-fold ($p < 0.001$) as early as 12 h, whereas RANKL expression was very low and was not found to be modulated by iCR. Of note, the stimulatory effect of iCR on OPG production was abrogated by the pure estrogen receptor antagonist ICI 182,780. Moreover, iCR enhanced two osteoblastic differentiation markers, bone-specific alkaline phosphatase activity and osteocalcin expression, by up to 4- and 3-fold, respectively ($p < 0.001$).

CONCLUSIONS: Our data suggest that iCR enhances differentiation and increases the OPG-to-RANKL ratio of normal human osteoblasts. These effects may contribute to the positive skeletal effects of black cohosh.