Evidence for selective estrogen receptor modulator activity in a black cohosh (Cimicifuga racemosa) extract: comparison with estradiol-17beta.

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OBJECTIVE: Some phytoestrogens are believed to have selective estrogen receptor modulator (SERM) activity with no action in the uterus but beneficial effects in the hypothalamo/pituitary unit and in the bone and are presently the focus of clinical interest. In the present experiments, the effects of the clinically used Cimicifuga racemosa (CR) extract BNO 1055 in the uterus, in the bone and on serum luteinizing hormone (LH) were compared with the effects of estradiol-17beta (E(2)) under acute and chronic conditions in ovariectomized rats. METHODS: Ovariectomized rats were treated either acutely (6 h) or chronically (3 Months) with E(2) or the CR extract. Gene expression of some estrogen-regulated genes in the metaphysis of the tibia and the uterus was determined. Furthermore, bone mineral density was measured by quantitative computer tomography. RESULTS: When given acutely, both E(2) and the CR extract inhibited LH secretion and slightly stimulated gene expression of IGF-I, collagen-1alpha1, osteoprotegerin and osteocalcin (all osteoblast products), and of tartrate-resistant acid phosphatase (TRAP, an osteoclast product) in the metaphysis of the femur. While E(2) stimulated uterine weight and expression of progesterone receptor (PR), the complement protein (C3) and IGF-I genes, and inhibited gene expression of the estrogen receptor beta (ERbeta) in the uterus, no such effect was observed under acute CR treatment. After chronic application with pelleted food over 3 Months E(2) had profound effects in the uterus on weight and gene expression (ERbeta, PR, C3 and IGF-I) which were not seen in the CR-treated animals. Within 3 Months after ovariectomy, control rats had lost more than 50% of the metaphyseal bone mass of the tibia, an effect prevented by E(2) and partially by CR supplementation. CONCLUSIONS: These data confirm the concept that the CR extract BNO 1055 contains as yet unidentified substances with SERM properties which act in the hypothalamo/pituitary unit and in the bone but not in the uterus.

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