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Inhibition of aromatase activity in MCF-7aro human breast cancer cells by the natural androgens testosterone and androstenedione

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Abstract

Background: The human breast contains all the enzymes responsible for local bioformation of estradiol (E_2). Two principal pathways are implicated in the last steps of E_2 formation: the 'aromatase' which transforms androgens into estrogens, and the 'sulfatase' which converts estrogen sulfates into active unconjugated estrogens; activities found in both normal and cancerous breast. Aromatase inhibition by anti-aromatase agents is largely used with very positive results in the treatment of breast cancer patients. In this study, the effects of the natural androgens androstenedione and testosterone were explored on aromatase activity in a stable aromatase-expressing estrogen receptor-positive human breast cancer cell line MCF-7aro.

Materials and methods: The cells were incubated with physiological concentrations of [^{3}H]-testosterone (5 nmol/L) alone or in the presence of either testosterone or androstenedione (0.5 and 50 µmol/L) 24 h at 37°C. Cellular radioactivity uptake was determined. [^{3}H]-E_2 was characterized by thin-layer chromatography.

Results: The MCF-7aro cells have a very high aromatase activity because conversion of [^{3}H]-testosterone to [^{3}H]-E_2 was 3.02±0.17 pmol/mg DNA in non-treated cells. Testosterone, at concentrations of 0.5 and 50 µmol/L, provoked inhibition of E_2 formation of 36% and 79%, respectively. The effect of androstenedione at 0.5 and 50 µmol/L was 56% and 76%, respectively.

Conclusion: In breast cancer cells, the natural androgens testosterone and androstenedione, have the capacity to control bioformation of estradiol by blocking aromatase activity. The data can provide important information on the control mechanism of estrogen intratumoral levels and open new possibilities in breast cancer treatment.

Keywords androgens, aromatase, breast cancer, estrogens, testosterone

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