Characterization of the Androgen-Sensitive MDA-kb2 Cell Line for Assessing Complex Environmental Mixtures

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Synthetic and natural steroidal androgens and estrogens and many other non-steroidal endocrine-active compounds commonly occur as complex mixtures in aquatic environments. It is important to understand the potential interactive effects of these mixtures to properly assess their risk. In these studies we used the MDA-kb2 cell line, a human breast cancer cell line with endogenous androgen receptors and a stably-transfected luciferase reporter gene construct to quantify the androgenic activity of seven environmentally relevant natural and synthetic androgens: 17β-trenbolone, dihydrotestosterone, methyltestosterone, testosterone, trendione, 17α-trenbolone, and androstenedione. We tested combinations of these androgens and compared the observed activity to expected androgenic activity based on a concentration addition model. Our analyses support the hypothesis that androgen receptor agonists cause additive responses in a mixture. Binary mixtures of 17β-trenbolone with 17β-estradiol or triclocarban (an anti-microbial found in the environment) were also tested. 17β-Estradiol induced androgenic activity, but only at concentrations 600-fold greater than those found in the environment. Triclocarban enhanced the activity of 17β-trenbolone. Additionally, three anti-androgens were each paired with three androgens of varying potencies. The relative potencies of the antagonists were a vinclozolin metabolite (M2) > procymidone > prochloraz regardless of the androgen used. The results of our studies demonstrate the potential utility of the androgen-responsive MDA-kb2 cell line for quantifying the activity of mixtures of endocrine-active chemicals in complex wastes such as municipal effluents and feedlot discharges.

Keywords: Concentration addition, (Anti)Androgen, Estrogen, Triclocarban

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