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Tamoxifen-Induced Apoptosis is Inhibited by Phthalates in Human Breast Cancer Cells

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Environmental estrogens represent a class of compounds which can mimic the function or activity of the endogenous estrogen 17β-estradiol (E2). Phthalates including butyl benzyl phthalate (BBP), di-(n-butyl) phthalate (DBP), and di-(2-ethylhexyl) phthalate (DEHP) are used as plasticizers, and also widely used in food wraps, toys, medical products and cosmetic formulations. Phthalates have been shown to mimic estrogen and are capable of binding to the estrogen receptor (ER). It has been demonstrated that estrogen promotes drug resistance to tamoxifen (TAM) in breast cancer. In order to further evaluate the potential role of the phthalates as environmental estrogens, the effect of phthalates was investigated on TAM-induced apoptosis in MCF-7 human breast cancer cells. Our results show that phthalates, BBP (100 mM), DBP (10 mM) and DEHP (10 mM), significantly increased cell proliferation in MCF-7, but not in MDA-MB-231 cells. In addition, BBP, DBP and DEHP mimiced estrogen in the inhibition of TAM-induced apoptosis in MCF-7 cells. Our data suggest that the inhibitory effect of phthalates on TAM-induced apoptosis involves an increase in intracellular Bcl-2 to Bax ratio. Given that the phthalates are widely used in cosmetics mainly for women, our findings which revealed the promoting effect of BBP, DBP and DEHP on chemotherapeutic drug resistance to TAM in breast cancer may be of biological relevance.

Keyword: endocrine disruptor, phthalate, MCF-7, tamoxifen, apoptosis