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Capsaicinoids are silent estrogens, a class of estrogenic chemicals without cell-proliferation activity

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ABSTRACT

Although environmental estrogens, including phytoestrogens, play important biological roles, their mechanisms of action are often not explored due to the lack of appropriate biological tools. For example, while capsaicin has been shown to exhibit various biological activities, its association with estrogenic cell signaling is mostly not well understood. We used an oligodeoxynucleotide-based DNA microarray containing estrogen-responsive genes to examine the gene expression profiles of capsaicinoids (capsaicin, dihydrocapsaicin, nordihydrocapsaicin and nonivamide) in human breast cancer MCF-7 cells to understand estrogenic signaling pathways at the transcription level, which was followed by Western blot analysis for signaling pathways at the protein level. While these capsaicinoids lacked cell-proliferation activity in MCF-7 cells, they showed expression profiles with high or moderate correlations (correlation coefficient or $R = 0.66$ to 0.83) with that of 17β-estradiol (E_2). Capsaicin seems to regulate the activation of Erk1/2 and PI3K/Akt through the pathways associated with both the epidermal growth factor receptor (EGFR) and the capsaicin receptor (TRPV1). In addition, capsaicin and E_2 differed in the regulation of cell cycle-related factors, such as cyclin D1 and $p27^{kip1}$. These results indicate that, while these capsaicinoids have estrogenic activity and are functionally similar to E_2, at both the transcriptional and protein levels, they lack the signaling for cell proliferation, and thus belong to silent estrogens, a class of estrogenic chemicals without cell-proliferation activity.