Estrogen Receptor Mediated Inhibition of NF-κB as a Route to Treatment of Breast Cancer

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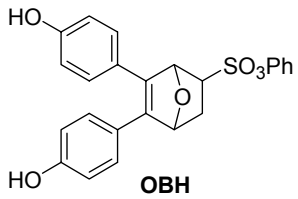
Breast cancer is the second most common cancer and second most fatal in women, leading to approximately 47,000 deaths in 2004. Breast cancers can result from overexpression of the estrogen receptor (ER). 60 – 70% of breast cancers are ER-positive, meaning they can respond to estrogen therapy. Unfortunately, treatment with the selective estrogen receptor modulator (SERM) tamoxifen leads to a recurrence of breast cancer. In these cases the ER undergoes functional changes that result in tamoxifen acting as an antagonist. *In vitro* studies suggest this may result from an interaction between the ER and NF-κB, a transcription factor which controls the production of interleukins responsible for cell proliferation. Oxabicyclic compound **OBH** binds with limited affinity to the estrogen receptor (RBA = 9%), but decreases the activity of NFκB. *In vitro* and *in vivo* studies have shown **OBH** has potential in breast cancer therapy. We will discuss the synthesis and biological activity of **OBH** and some analogs.



OBH