4-Hydroxyestradiol

National Cancer Institute

Source

National Cancer Institute. 4-Hydroxyestradiol. NCI Thesaurus. Code C120473.

A metabolite formed during the metabolism of 17beta-estradiol by hydroxylation of the carbon at position 4 by cytochrome P450 1B1, with potential carcinogenic activity. The mechanism of action for the tumor promoting activity of 4-hydroxyestradiol (4-OHE2) is not entirely known but this metabolite undergoes metabolic redox cycling with its oxidized quinoid form, estradiol 3,4-quinone, and generates reactive oxygen species (ROS), which induce oxidative DNA damage. 4-OHE2 also activates nuclear factor-kappaB (NF-kB) and extracellular signal-regulated kinase/mitogen-activated protein kinase pathways, and induces the expression of certain genes through activation of the estrogen receptor (ER), which stimulates cellular proliferation in susceptible cells.