

## Product Information

### 4-Hydroxytamoxifen

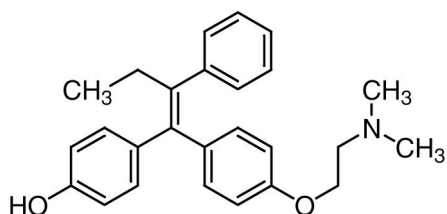
Product Numbers **H 7904**, **H 6278**

Storage Temperature 2-8 °C

CAS RN: 68047-06-03

Synonyms: ICI 79280; trans-4-[1-(4-[2-(Dimethylamino)ethoxy]phenyl)-2-phenyl-1-butenyl]phenol; 4-OHT

#### Product Description



Molecular formula: C<sub>26</sub>H<sub>29</sub>NO<sub>2</sub>

Molecular weight: 387.51

Method of preparation: Synthetic. Methods of synthesis have been reported.<sup>1-3</sup>

**H 7904**: minimum 98% of Z-isomer

**H 6278**: minimum 70% Z-isomer

4-Hydroxytamoxifen (4-OHT) is a metabolite of the antiestrogen, tamoxifen, in humans and other mammals. Both the Z (trans) and E (cis) 4-OHT isomers are antiestrogens in the immature rat. Based on studies of the structure-function relationships of fixed ring systems, it was found that the trans isomer is a potent antiestrogen and that the cis-isomer is a relatively weak (100X less) antiestrogen in T47D breast cancer cells in vitro.<sup>4,5</sup>

4-OHT has a higher affinity than tamoxifen and its other metabolites for binding to estrogen receptors and therefore has 50-100-fold greater potency of inhibiting cell multiplication in normal human breast cells<sup>6</sup> as well as in breast cancer cell lines in culture.<sup>7,8</sup> 4-OHT was effective in inhibiting growth in these cells in the absence of estrogen when cell proliferation was stimulated by insulin or epidermal growth factor.<sup>8</sup>

4-OHT and tamoxifen were reported to be intramembranous inhibitors of lipid peroxidation and to

exhibit peroxy radical scavenging activity.<sup>9</sup> A concentration of 25 M 4-OHT almost completely prevented the oxidation of cis-parinaric acid.<sup>9</sup> 4-OHT is a better inhibitor of microsomal lipid peroxidation and of liposomal peroxidation than tamoxifen, 3-hydroxytamoxifen, or 17 $\beta$ -estradiol.<sup>10</sup>

Tamoxifen and 4-hydroxytamoxifen were found to induce depolarization of the mitochondrial membrane potential ( $\Delta\psi$ ) and uncouple the mitochondrial respiration, depressing the oxidative phosphorylation efficiency in rat liver mitochondria. Both drugs caused a decrease in mitochondrial ATP level.<sup>11</sup> In addition 4-OHT was found to protect against oxidative stress in brain mitochondria.<sup>12</sup>

Tamoxifen and 4-hydroxytamoxifen markedly induce cytochrome P450 3A4, a drug-metabolizing enzyme of central importance, in primary cultures of human hepatocytes.<sup>13</sup> 4-OHT, tamoxifen and other metabolites in biological systems have been analyzed by HPLC and GC-mass spectrometry.<sup>14,15</sup>

#### Precautions and Disclaimer

This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

#### Preparation instructions

Soluble in ethanol, 20 mg/ml (with heating) and in methanol, 10 mg/ml, producing a clear faint yellow solution. Solutions should be stored protected from light at -20 °C.

4-OHT undergoes a cis-trans (E-Z) interconversion process favored by solvents of low dielectric constants when exposed to light and when incubated in culture medium.<sup>1,16</sup> This isomerization occurs in all common laboratory solvents but can be prevented by storage of the compound in tetrahydrofuran containing about 0.025% butylated hydroxytoluene (BHT) at -25 °C in the dark. These solutions should be stable for about 6 months with less than 5% loss in isomeric purity.<sup>1</sup>

### Storage/Stability

Store desiccated and protected from light at 2-8 °C.  
Under these conditions the product is stable for 3 years.

### References

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