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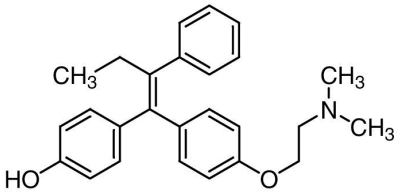
Product Information

4-Hydroxytamoxifen

Catalog Numbers **H7904 and H6278**
Storage Temperature 2–8 °C

CAS RN
68047-06-3 (Z isomer)
68392-35-8 (unspecified isomer)
Synonyms: ICI 79280, 4-OHT, *trans*-4-[1-(4-[2-(Dimethylamino)ethoxy]phenyl)-2-phenyl-1-butenyl]phenol

Product Description



Molecular formula: $C_{26}H_{29}NO_2$
Molecular weight: 387.51

Method of preparation: Synthetic, methods of synthesis have been reported.[1-3]
Catalog **H7904**: ≥98% Z isomer
Catalog **H6278**: ≥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 the *cis* isomer is a relatively weak (100× less) antiestrogen in T47D breast cancer cells *in vitro*.[4,5]

4-OHT has a higher affinity than tamoxifen and its other metabolites for binding to estrogen receptors and therefore, has 50 to 100-fold greater potency of inhibiting cell multiplication in normal human breast cells[6] as well as in breast cancer cell lines in culture.[7,8] 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.[8]

4-OHT and tamoxifen were reported to be intramembranous inhibitors of lipid peroxidation and to exhibit peroxyl radical scavenging activity.[9] A concentration of 25 μM 4-OHT almost completely prevented the oxidation of *cis*-parinaric acid.[9] 4-OHT is a better inhibitor of microsomal lipid peroxidation and of liposomal peroxidation than tamoxifen, 3-hydroxy-tamoxifen, or 17β-estradiol.[10]

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.[11] In addition 4-OHT was found to protect against oxidative stress in brain mitochondria.[12]

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

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 clear faint yellow solutions. 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.[1,16] This isomerization occurs in all common laboratory solvents, but can be prevented by storage of the compound in tetrahydrofuran containing ~0.025% butylated hydroxytoluene (BHT) at –25 °C in the dark. These solutions should remain active for ~6 months with <5% loss in isomeric purity.[1]

Storage/Stability

Store desiccated and protected from light at 2–8 °C. Under these conditions the product remains active for 3 years.

References

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EM,NDH,PHC,MAM 12/11-1