Endoxifen hydrochloride

Cat. No.: HY-18719B

CAS No.: 1197194-41-4

Molecular Formula: $C_{25}H_{28}ClNO_2$

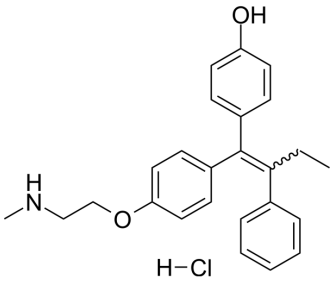
Molecular Weight: 409.95

Target: Estrogen Receptor/ERR; Drug Metabolite; Parasite; Cytochrome P450

Pathway: Vitamin D Related/Nuclear Receptor; Metabolic Enzyme/Protease; Anti-infection

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 35 mg/mL (85.38 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4393 mL	12.1966 mL	24.3932 mL
5 mM	0.4879 mL	2.4393 mL	4.8786 mL
10 mM	0.2439 mL	1.2197 mL	2.4393 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.10 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Endoxifen hydrochloride is a key active metabolite of Tamoxifen (TAM) with higher affinity and specificity to estrogen receptor that also inhibits aromatase activity. Endoxifen hydrochloride has the potential for breast cancer study[1][2].

IC_{50} & Target

Aromatase

In Vitro

Endoxifen, a hydroxylated Tamoxifen metabolite, is approximately 100-fold more potent as an antagonist of the ER than tamoxifen. It also suggests that endoxifen but not 4-hydroxytamoxifen results in ER-alpha degradation in addition to its effects on the ER at the level of transcription[1]. Endoxifen, is a potent antiestrogen that targets estrogen receptor α for degradation in breast cancer cells. Additionally, it is showed that Endoxifen blocks ERA transcriptional activity and inhibits

	estrogen-induced breast cancer cell proliferation even in the presence of tamoxifen, N-desmethyl-tamoxifen, and 4-hydroxytamoxifen[2]. Endoxifen is strongly growth inhibitory at 10 μM for all the breast cancer cell lines except for moderate inhibition for MDAMB-468.Cytotoxic effects are quite significant at 10 μM concentration for MCF7, HS 578T, and BT-549 cells. At lower Endoxifen concentrations (0.01-1 μM), the inhibitory effects are not as significant as 10 μM, whereas 100 μM Endoxifen concentration found to be lethal for all tested cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Orally administered Endoxifen is rapidly absorbed and systemically available when tested in female rats. The Endoxifen-treated rats show 787% higher exposure ($AUC_{0-\infty}$) and 1,500% higher concentration (C_{max}) levels of Endoxifen when compared with Tamoxifen. Oral Endoxifen administration once a day for 28 consecutive days at dosages 2, 4, and 8 mg/kg proves safe and results in progressive inhibition of the growth of the human mammary tumor xenografts in female mice[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice[2] Six-weeks-old, female, athymic NCr–nu/nu mice are implanted subcutaneously (s.c.) near the right flank with 30-40-mg fragment of MCF-7 human mammary tumor from an in vivo passage. The day of tumor fragments implantation is designated as Day 0. To support the estrogen-dependent MCF-7 tumor growth, each animal is implanted s.c. in the back of the neck with a 0.72-mg 17 β-estradiol 60-day release pellet 1 day prior to tumor fragment implantation. Individual tumors grew to 75-196 mm^3 in size on Day 13 after tumor fragment implantation, the day of treatment initiation. A total of 36 tumor bearing mice are randomized and divided into 4 treatments (6 mice/group) and one control (12 mice/group) groups. At day 13 post tumor implantation, treatment with control (water), Endoxifen at three dose levels (2, 4, and 8 mg/kg) or Tamoxifen twice a day, 3 h apart at a dosage of 10 mg/kg are administered by oral gavage once daily for 28 consecutive days. The dose volume 0.2 mL/10 g body weight is kept constant for all treatment groups. The s.c. tumors are measured and the animals are weighed twice weekly starting on the first day of treatment. The study is terminated on Day 58. The median time to reach two tumor mass doublings is used in the calculation of the overall delay in the growth of the median tumor. Additionally, comparison of the median tumor weight in the treatment groups to the median tumor weight in the control group (T/C 9 100%) on Day 41 (1 day after the last treatment) and on Day 58 (the day of study termination) are used for an additional evaluation of the antitumor efficacy[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Wu X, et al. The tamoxifen metabolite, Endoxifen, is a potent antiestrogen that targets estrogen receptor alpha fordegradation in breast cancer cells. Cancer Res. 2009 Mar 1;69(5):1722-7.

[2]. Goetz MP, et al. Tamoxifen, endoxifen, and CYP2D6: the rules for evaluating a predictive factor. Oncology (Williston Park). 2009 Dec;23(14):1233-4, 1236.

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