MP Biomedicals, LLC

29525 Fountain Parkway
Solon, Ohio 44139

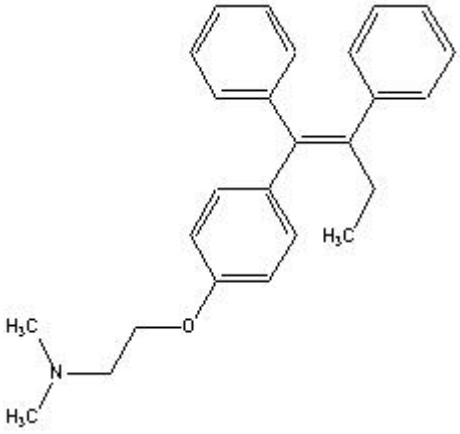
Telephone: 440/337-1200
Toll Free: 800/854-0530
Fax: 440/337-1180
mailto: biotech@mpbio.com
web: http://www.mpbio.com

TECHNICAL INFORMATION

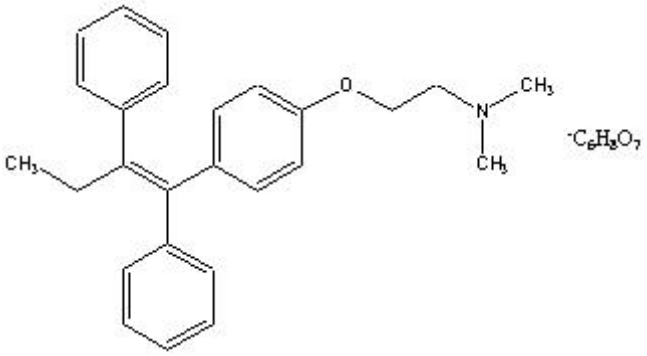
Catalog Number: 156738, 156739
Tamoxifen

Structure:

Free Base



Citrate Salt



	Free Base	*Citrate Salt*
Molecular Formula	$C_{26}H_{29}NO$	$C_{26}H_{29}NO \cdot C_6H_8O_7$
Molecular Weight	371.5	563.6
CAS #	10540-29-1	54965-24-1

Synonyms: [Z]-1-[p-Dimethylaminoethoxyphenyl]-1,2-diphenyl-1-butene; (Z)-2-[4-(1,2-Diphenyl-1-butenyl)phenoxy]-N,N-dimethylethanamine; ICI 47699; trans-Tamoxifen; Z-Tamoxifen; (Z)-2-(p-(1,2-Diphenyl-1-butenyl)phenoxy)-N,N-dimethylethylamine; trans-1-(p-b-Dimethylaminoethoxyphenyl)-1,2-diphenylbut-1-ene citrate
Physical Description: White fine, crystalline powder
pKa: approximately 8.85[4]; approximately 6.9 (in Triton® X-100)[7,9]
Stability: Tamoxifen is hygroscopic at high relative humidities and is senstive to UV light.[1,14] It is recommended to store the products in the dark.
Solubility:

Free Base: Practically insoluble in water (< 0.01% @ 20°C); soluble in methanol, ethanol, 2-propanol, propylene glycol, chloroform (50 mg/ml - clear, colorless to faint yellow solution) or DMSO. Solutions are sensitive to UV light. Photolysis products are the E isomer and the phenanthrenes formed by cyclization of both isomers.[14] Solutions in DMSO may be stable when stored at -20°C in the dark.[26]
Citrate Salt: Soluble in methanol (50 mg/ml with heat) or ethanol (10 mg/ml with sonication); very slightly soluble in water (0.3 mg/L @ 20°C; the pH is approximately 3.0-3.5), 0.02 N HCl (0.2 mg/ml @ 37°C)[4], acetone or chloroform. A 4.0 mM solution in DMSO can be prepared.[7] Solutions are sensitive to UV light. Photolysis products are the E isomer and the phenanthrenes formed by cyclization of both isomers.[14]

Description: Protein kinase C inhibitor (IC_{50} = 50-200 uM depending on assay conditions[29] in MCF-7 cells[17] or IC_{50} = 100 uM in rat brain[26]). The PKC inhibition is also dependent on the phospholipid concentration. Also inhibits both calmodulin-dependent and calmodulin-independent Ca^{2+}-, Mg^{2+}-ATPase.
Induces apoptosis in human malignant glioma cell lines. Tamoxifen and its metabolite 4-hydroxytamoxifen are mixed estrogen agonists/antagonists.
Tamoxifen has been shown to protect bone from estrogen-deficiency bone loss and lower plasma cholesterol in the rat.[15] A 10 uM solution has exhibited fungicidal activity (optimal pH 7.5) against yeast cells of *C. albicans*.[7] It has been implemented in liver carcinogenesis in rats.[16] A possible mechanism for the DNA adduct formation leading to carcinogenesis was reported.[22] 100 nM solutions combined with vinblastine are cytotoxic to both rat prostate adenocarcinoma cell line and human prostate cancer cells.[27] Flow cytometric analysis of DNA content and BrdU (5-bromo-2'-deoxyuridine) labeling in MCF-7 (estrogen-responsive human clonal breast cancer cell line) cells have shown that the effect of tamoxifen on the growth of estrogen-dependent cells in culture

may be due to accumulation of cells in G1 phase (before onset of S-phase) and the exit of some cells from the cycling compartment in the cell cycle progress.[11] The mechanism of tamoxifen action may involve interactions in the signaling transduction pathway: tamoxifen is a competitive inhibitor of calmodulin-stimulated phosphodiesterase activity; molecular interactions between tamoxifen and calmodulin were reported.[13]
Other actions of tamoxifen are:

– Reduction of plasma levels of insulin-like growth factor;
– Induction of cells surrounding cancer cells to secrete transforming growth factor b;
– Inhibition of membrane lipid peroxidation probably by decreasing membrane fluidity.[33]

Availability:

Catalog Number	Description	Size
156738	Tamoxifen, free base	100 mg 250 mg 1 g
156739	Tamoxifen, citrate salt	100 mg 250 mg 1 g

References:

– *Merck Index* **12th Ed.**, No. 9216.
– Goodman and Gilman's *The Pharmacological Basis of Therapeutics,* **7th Ed.,** 1297, 1424 (1985).
– *Martindale, The Extra Pharmacopoeia,* **30th Ed.,** p. 500 (1993).
– *Physicians' Desk Reference,* **47th Ed.,** 1126 (1993).
– Adam, H.K., *Non-Steroidal Antioestrogens: Mol. Pharmacol. Antitumor Act.*, Sutherland, R.L. and Jordan, V.C. (eds.), Academic Press: Sydney, Australia, p. 59 (review) (1981).
– Al-Hassan, M.I., *Synth. Commun.*, **v. 17**, 1247 (1987).
– Beggs, W.H.J., *Antimicrob. Chemother.*, **v. 37**, 841 (1996).
– Berthou, F. and Dreano, Y., *J. Chromatogr.*, **v. 616**, 117 (1993).
– Bottega, R. and Epand, R.M., *Biochem.*, **v. 31**, 9025 (1992).
– Buckley, M.M.T. and Goa, K.L., *Drugs*, **v. 37**, 451 (1989) (review).
– Danova, M., et al., *Annals NY Acad. Sci.*, **v. 698**, 174 (1993).
– Duax, W.L., et al., *Environ. Health Perspect.*, **v. 61**, 111 (1985).
– Edwards, K.J., et al., "A molecular modeling study of the interactions between the antiestrogen drug tamoxifen and several derivatives, and the calcium-binding protein calmodulin." *J. Med. Chem.*, **v. 35**, 2753-2761 (1992).
– Furr, B.J.A. and Jordan, V.C., *Pharmacol. Ther.*, **v. 25**, 127 (1984).
– Gold, E., et al., "Tamoxifen and norethisterone: effects on plasma cholesterol and total body calcium content in the estrogen-deficient rat." *Horm. Metab. Res.*, **v. 26**, 100-103 (1994).
– Han, X. and Liehr, J.G., *Cancer Res.*, **v. 52**, 1360 (1992).
– Issandou, M., et al., "Opposite effects of tamoxifen on in vitro protein kinase C activity and endogenous protein phosphorylation in intact MCF-7 cells." *Cancer Res.*, **v. 50**, 5845-5850 (1990).
– Jalonen, H.G.J., *Pharm. Sci.*, **v. 77**, 810 (1988).
– Jordan, V.C., et al., *Mol. Cell. Endocrinol.*, **v. 7**, 177 (1977).
– Jordan, V.C., *Breast Cancer Res. Treat.*, **v. 2**, 123 (1982) (review).
– Jordan, V.C., *Annu. Rev. Pharmacol. Toxicol.*, **v. 35**, 195 (1995).
– Kuramochi, H., *J. Med. Chem.*, **v. 39**, 2877 (1996).
– Lau, C.K., et al., *Proc. Natl. Acad. Sci. USA*, **v. 88**, 829 (1991).
– Murphy, C., et al., *J. Steroid Biochem.*, **v. 26**, 547 (1987).
– Nicholson, R.I. and Griffiths, K., *Advances in Sex Hormone Res.*, **v. 4**, 119 (1980).
– O'Brian, C.A., et al., "Inhibition of protein kinase C by tamoxifen." *Cancer Res.*, **v. 45**, 2462-2465 (1985).
– Pienta, K.J., et al., "Inhibition of prostate cancer growth by vinblastine and tamoxifen." *Prostate*, **v. 26**, 270-274 (1995).
– Precigoux, G., et al., *Acta Cryst.*, **B35**:3070 (1979).
– Powis, G., "Signalling targets for anticancer drug development." *Trends Pharmacol. Sci.*, **v. 12**, 188-194 (1991).
– Sastry, C.S.P., et al., *Talanta*, **v. 42**, 1479 (1995).
– Sastry, C.S.P. and Lingeswara Rao, J.S.V.M., *Indian J. Pharm. Sci.*, **v. 57**, 133 (1995).
– Weir, P.J., et al., *J. Pharm. Biomed. Anal.*, **v. 7**, 393 (1989).
– Wiseman, H., "Tamoxifen and estrogens as membrane antioxidants: comparison with cholesterol." *Meth. Enzymol.*, **v. 234**, 590-602 (1994).
– "Pharmacokinetics and bioavailability of tamoxifen in postmenopausal healthy women." *Arzneimittelforschung*, **v. 46:4**, 418-422 (1996).
– "Effects of tamoxifen and levonorgestrel treatment on carbon tetrachloride induced alterations in rats." *Arzneimittelforschung*, **v. 41:12**, 1298-1301 (1991).
– "In vitro growth promotion of human mammary carcinoma cells by steroid hormones, tamoxifen, and prolactin." *J. Natl. Cancer Inst.*, **v. 73:2**, 313-321 (1984).
– "The endometrium in breast cancer patients on tamoxifen." *Arch. Gynecol. Obstet.*, **v. 263:4**, 170-177 (2000).
– "Tamoxifen effects on endometrium." *Panminerva Med.*, **v. 42:1**, 45-47 (2000).
– "Differences in immunoreactivity of estrogen receptor (ER) in tamoxifen-sensitive and -resistant breast carcinomas: preclinical and first clinical investigations." *Breast Cancer Res. Treat.*, **v. 60:1**, 81-92 (2000).
– "Breast cancer genetics and the role of tamoxifen in prevention." *J. Am. Acad. Nurse Pract.*, **v. 12:1**, 21-28; quiz 29-31 (2000).

– "Tamoxifen decreases renal inflammation and alleviates disease severity in autoimmune NZB/W F1 mice." *Scand. J. Immunol.* , **v. 52:4**, 393-400 (2000).
– "Tamoxifen inhibits lipoprotein activity: in vivo and in vitro studies." *Horm. Res.*, **v. 53:1**, 36-39 (2000).
– "Endometrial metastasis from breast cancer in a patient receiving tamoxifen therapy." *Gynecol. Obstet. Invest.*, **v. 50:2**, 136-138 (2000).
– "Effect of tamoxifen pretreatment on the pharmacokinetics, metabolism and cardiotoxicity of doxorubicin in female rats." *Cancer Chemother. Pharmacol.*, **v. 46:3**, 185-192 (2000).