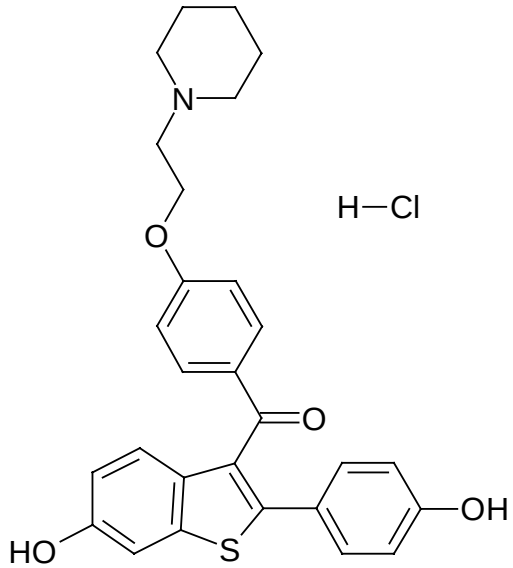
ProductInformation

RALOXIFENE HYDROCHLORIDE

Product Number **R 1402**
Storage Temperature: RT

CAS#: 84449-90-1
Synonyms: [6-Hydroxy-2-(4-hydroxyphenyl)-benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]; LY 139,481; Keoxifene



Product Description
Molecular Formula: $C_{28}H_{27}NO_4S \bullet HCl$
Molecular Weight: 510.05

Supplied as a light yellow solid.
Purity: >99% (HPLC)
Melting Point: 267.3-268.5 °C

Selective estrogen receptor modulators (SERMs) constitute a family of compounds that demonstrate tissue selective estrogenic and antiestrogenic activities. Raloxifene belongs to the benzothiophene class of antiosteoporotic compounds. It binds to the nuclear estrogen receptors (ERα and ERβ) and either activates or blocks ER-induced gene transmission, depending on the tissue involved. Raloxifene demonstrates estrogen agonist effects on bone and blood lipid levels while it is a competitive antagonist of estrogen at mammary and uterine estrogen receptors.[1,2]

Raloxifene has been shown to protect bone from estrogen-deficiency bone loss. Both raloxifene and estrogen inhibit mammalian osteoclast differentiation and bone resorption in the presence of IL-6 *in vitro*. Raloxifene and estrogen also induce similar activation of TGF-β_3, a cytokine associated with inhibition of osteoclast differentiation and activity in ovariectomized rats.[3] Raloxifene is cardioprotective, in part due to its effects on plasma lipid distribution. Like estradiol, raloxifene reduces total and low-density lipoprotein (LDL) levels in plasma. However, unlike estradiol, it does not increase plasma high-density lipoprotein (HDL) and triglyceride levels in plasma.[2,4]

Raloxifene reduces both the incidence of experimental mammary carcinogenesis *in vivo*[5] and the proliferation of estrogen-dependent mammary tumor cells *in vitro*.[6] In intact animals, estrogens provide negative feedback regulation of the release of tropic hormone releasing factors and tropic hormones from the hypothalamus and anterior pituitary, respectively. Recent studies indicate that raloxifene blocks the action of estrogens on hypothalamic and pituitary cells of intact female rats[7] and inhibits estradiol-mediated induction of progesterone receptor mRNA in an immortalized rat embryonic hypothalamic cell line.[1] However, in ovariectomized females raloxifene acts as an ER agonist, in that it reduces luteinizing hormone (LH) release and stimulates prolactin secretion.[7]

Preparation Instructions
Raloxifene is soluble in DMSO, at 28 mg/ml. It is insoluble in water.

Storage/Stability
Store tightly sealed at room temperature. Raloxifene is stable for at least two years when stored appropriately.

References

1. Fitzpatrick, S. L., et al., Effect of estrogen agonists and antagonists on induction of progesterone receptor in a rat hypothalamic cell line., Endocrinology, **140**, 3928-3937 (1999).
2. Bryant, H. U., Mechanism of action and preclinical profile of Raloxifene, a selective estrogen receptor modulator., Rev. Endocr. Metab. Disord., **2,** 129-138 (2001
3. Bryant, H.U., et al., An estrogen receptor basis for raloxifene action in bone. J Steroid Biochem. Mol. Biol., **69**, 37-44 (1999).

4. Saitta, A., et al., Cardiovascular effects of Raloxifene hydrochloride., Cardiovasc. Drug Rev., **19,** 57-74 (2001).
5. Kubatka, P., et al., Preventive effects of Raloxifene and melatonin in N–methyl–N–nitrosourea–induced mammary carcinogenesis in female rats., Neoplasma, **48,** 313-319 (2001).
6. Wolczynski, S., et al., Estrogenic and antiestrogenic effects of raloxifene on collagen metabolism in breast cancer MCF-7 cells. Gynecol. Endocrinol., **15**, 225-233 (2001).
7. Pinilla, L., et al., Evidence of an estrogen-like action of Raloxifene upon the hypothalamic–pituitary unit: Raloxifene inhibits lutenizing hormone secretion and stimulates profilactin secretion in ovariectomized female rats., Neurosci. Lett., **311,** 149-152 (2001).

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