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\textsubscript{28}H\textsubscript{27}NO\textsubscript{4}S •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 (ER\(\alpha\) and ER\(\beta\)) 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 \textit{in vitro}.\(^{2}\)

Raloxifene and estrogen also induce similar activation of TGF-\(\beta_3\), 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.\(^{24}\)

Raloxifene reduces both the incidence of experimental mammary carcinogenesis \textit{in vivo}\(^5\) and the proliferation of estrogen-dependent mammary tumor cells \textit{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

\[\text{HO} \quad \text{H} \quad \text{Cl} \quad \text{N} \quad \text{O} \quad \text{S} \quad \text{C}_\text{28} \text{H}_\text{27} \text{NO}_4 \text{S} \quad \text{HCl}\]


AH/LY 2/02