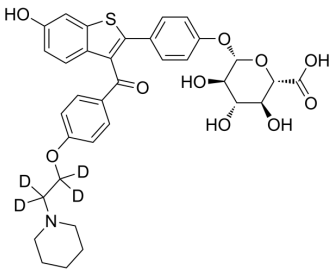
Raloxifene 4'-glucuronide-d4

Cat. No.:	HY-135582S
CAS No.:	1279033-52-1
Molecular Formula:	$C_{34}H_{31}D_4NO_{10}S$
Molecular Weight:	653.73
Target:	Estrogen Receptor/ERR; Isotope-Labeled Compounds
Pathway:	Vitamin D Related/Nuclear Receptor; Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Raloxifene 4'-glucuronide-d_4 is deuterated labeled Raloxifene 4'-glucuronide (HY-135582). Raloxifene 4'-glucuronide is a primary metabolite of Raloxifene. Raloxifene 4'-glucuronide formation is mediated mostly by UGT1A10 and UGT1A8. Raloxifene 4'-glucuronide binds to estrogen receptor with an IC_{50} of 370 μM. [1][2]. Raloxifene is a selective estrogen receptor modulator. Raloxifene activates TGFβ3 promoter as a full agonist at nanomolar concentrations, and inhibits the estrogen response element-containing vitellogenin promoter expression[3].
In Vitro	Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug molecules, largely as tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to affect the pharmacokinetic and metabolic profiles of drugs[1]. Expressed UGT1A8 catalyzes Raloxifene 4'-glucuronide with an apparent K_m of 59 μM and a V_{max} of 2.0 nmol/min/mg. Based on rates of Raloxifene glucuronidation and known extrahepatic expression, UGT1A8 and 1A10 appear to be primary contributors to Raloxifene glucuronidation in human jejunum microsomes. For human liver microsomes, the variability of Raloxifene 4'-glucuronide formation is 4-fold. Treatment of expressed UGTs with alamethicin results in minor increases in enzyme activity, whereas in human intestinal microsomes, maximal increases of 9-fold for the Raloxifene 4'-glucuronide are observed. Intrinsic clearance values in intestinal microsomes are 95 μl/min/mg for the Raloxifene 4'-glucuronide[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Izgelov D, et al. The Effect of Piperine Pro-Nano Lipospheres on Direct Intestinal Phase II Metabolism: The Raloxifene Paradigm of Enhanced Oral Bioavailability. Mol Pharm. 2018 Apr 2;15(4):1548-1555.

[2]. Kemp DC, et al. Characterization of raloxifene glucuronidation in vitro: contribution of intestinal metabolism to presystemic clearance. Drug Metab Dispos. 2002 Jun;30(6):694-700.

[3]. Yang NN, et al. Estrogen and raloxifene stimulate transforming growth factor-beta 3 gene expression in rat bone: a potential mechanism for estrogen- or raloxifene-mediated bone maintenance. Endocrinology. 1996 May;137(5):2075-84.

[4]. Russak EM, et al. Impact of Deuterium Substitution on the Pharmacokinetics of Pharmaceuticals. Ann Pharmacother. 2019 Feb;53(2):211-216.

Caution: Product has not been fully validated for medical applications. For research use only.

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