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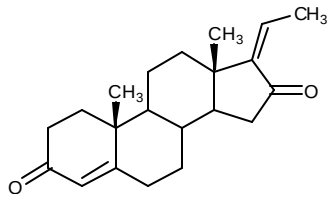
ProductInformation

(Z)-Guggulsterone

Catalog Number **G5168**
Storage Temperature: 2–8 °C

CAS RN: 39025-23-5

Synonyms: (17Z)-Pregna-4,17(20)-diene-3,16-dione; 4,17(20)-cis-Pregnadiene-3,16-dione



Product Description

Molecular Formula: $C_{21}H_{28}O_2$
Molecular Weight: 312.45

The bile acid receptor FXR is a promiscuous nuclear hormone receptor that controls expression of critical genes in bile acid and cholesterol homeostasis. According to recent studies, FXR inhibits expression of cholesterol 17α-hydroxylase, sterol 12α-hydroxylase, the Na^+/taurocholate co-transporting polypeptide and apolipoprotein A-I. In addition it activates expression of intestinal bile acid-binding protein (I-BABP), phospholipid transfer protein, bile salt export pump (BSEP), dehydroepiandrosterone sulfotransferase and apolipoprotein C-II.[1-4]

The resin of the guggul tree *Commiphora mukul* has been widely used to treat a wide variety of ailments, including obesity and lipid disorders. The active ingredients of the resin extract are stereoisomers E-and Z-guggulsterone, which activate FXR and directly decrease hepatic cholesterol levels. In transient transfections of mouse hepatocyte cells with a synthetic FXR responsive reporter plasmid, (Z)-guggulsterone alone had no effect on FXR activity, but it strongly inhibited FXR activation by chenodeoxycholic acid (CDCA), the most potent of the bile acid agonists.[5] In the presence of 100 µM CDCA, (Z)-guggulsterone at 10 µM decreased FXR transactivation by nearly 50% and at 100 µM resulted in 90% inhibition.[5]
Very similar results were observed recently with the promoter of the orphan receptor SHP, which contains an FXR-retinoid X receptor (FXR-RXP) heterodimer binding site and is induced by bile acids.[6]
Guggulsterone does not activate or inhibit transactivation by several other receptors associated with lipid metabolism, including liver X receptor a (LXRa), peroxisome proliferator activated receptor ? (PPAR?) and RXRα.[5]

Guggulsterone, although acting as an FXR antagonist in coactivator association assays, enhances FXR agonist-induced transcription of bile salt export pump (BSEP), a major hepatic bile acid transporter. In the presence of an FXR agonist such as CDCA or GW4064, guggulsterone enhanced endogenous BSEP expression in HepG2 cells with a maximum induction of 400-500% that of an FXR agonist alone.[4] Expression of SHP was also significantly increased, whereas expression of other FXR targets remained unchanged. Guggulsterone, a selective bile acid receptor modulator (SBARM), may represent a new class of FXR ligands that antagonize FXR agonist-induced coactivator recruitment in coactivator association assays but selectively enhance FXR target expression in cells and animals.[4]

Precautions and Disclaimer

This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

Preparation Instructions

Soluble in DMSO at 5 mg/ml.

References

1. Parks, D. J., et., al., *Science*, **284**, 1365-1368 (1999).
2. Sinal, C. J., et al., *Cell*, **102**, 731-744 (2000).
3. Singh, R. B., et al., *Cardiovasc. Drugs Ther.*, **8**, 659-664 (1994).
4. Cui, J., et., al., *J. Biol. Chem*., **278**, 10214-10220 (2003).
5. Urizar, N. L., et al., *Science*, **296**, 1703-1706, (2002).
6. Lu, T. T., et al., *Mol. Cell*, **6**, 507-515 (2000).

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