(Z)-Guggulsterone

Catalog Number G5168
Storage Temperature: 2–8 ºC

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: C21H28O2
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-III.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

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