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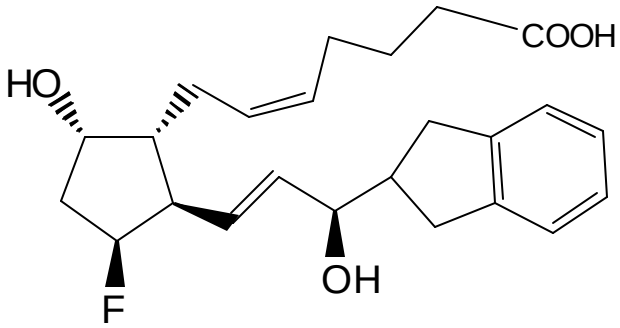
ProductInformation

AL-8810

Product Number **A 3846**
Storage Temperature 2-8 °C

CAS #: 246246–19–5
Synonyms: (5Z,13E)-(9S,11S,15R)-9,15-Dihydroxy-11-fluoro-15-(2-indanyl)-16,17,18,19,20-pentanor-5,13-prostadienoic acid



Product Description
Molecular Formula: $C_{24}H_{31}FO_4$
Molecular Weight: 402.51
Appearance: off-white semi solid
Purity: >98% by normal phase HPLC

AL-8810 is a prostaglandin $F_{2\alpha}$ analog and a selective FP prostanoid receptor antagonist. Prostaglandins (PGs) and thromboxanes (TXs) are metabolites of arachidonic acid that, together, comprise the prostanoids. Prostanoid receptors are classified on the basis of sensitivity toward the five naturally-occurring prostanoids: PGD_2, PGE_2, PGF_2, PGI_2 and TXA_2 and are termed P receptors, with a preceding letter indicating the natural prostanoid to which each receptor is most sensitive, i.e. DP, EP, FP IP and TP, respectively. All prostanoid receptors identified to date belong to the family of proteins characterized by having seven-transmembrane domains that couple to specific G proteins that initiate processes leading to the formation of the second messengers cAMP, inositol trisphosphate or diacylglycerol.[1]

FP receptors are potent and highly efficacious in reducing elevated intraocular pressure in dog and human models, in mediating luteolysis in *corpus luteum* of many species, and in inducing bronchoconstriction in cat and dog models. Agonist binding to the FP receptor activates phospholipase C (PLC), producing elevated levels of diacylglycerol and inositol trisphosphate; the latter induces a rapid increase in intracellular calcium. The major FP receptor isoform has high sequence homology among many animal species. However, the tissue distribution of the FP receptor varies between the species. Potent and selective FP receptors agonists have been available for many years, but until recently no well characterized, potent and selective FP antagonists have been identified.[2,3,4]

AL-8810 exhibits potent and selective antagonist properties at the FP prostanoid receptor. This action of AL–8810 was measured by the inhibition of fluprostenol-stimulated phosphatidylinositol (PI) turnover in Swiss mouse 3T3 fibroblasts and in A7r5 rat vascular smooth muscle cells. Preincubation of A7r5 cells with increasing concentrations of AL–8810 (10^{-11}–10^{-5} M) induced a dose-dependent inhibition of the increase in PI turnover induced by the subsequent addition of 100 nM fluprostenol, a highly selective full agonist at the FP receptor. The mean antagonist potency (K_i) of AL–8810 at the FP prostanoid receptor in both 3T3 fibroblasts and A7r5 vascular smooth muscles cells was 400-500 nM. AL–8810 produced a concentration-dependent shift in the fluprostenol concentration-response curve, without significantly decreasing the maximal response, indicating that AL–8810 is a competitive antagonist. Al–8810 also exhibited similar antagonist potency in inhibiting fluprostenol-stimulated PLC activation in HEK-293 cells expressing the cloned human ocular FP receptor. In contrast, even at 10 µM concentration, AL-8810 did not significantly inhibit DP, EP_2, EP_4 and IP prostanoid receptors.[5] In other studies, AL-8810 fully blocked the intracellular calcium mobilization in human embryonic kidney cells induced by the potent FP prostanoid receptor agonist, bimatoprost.[6]

AL–8810 is a valuable tool for determining specific FP receptor-mediated functions in complex biological systems.

Preparation Instructions

AL–8810 is soluble in DMSO at >10 mg/ml. It is also soluble in ethanol.

Storage/Stability

Store under nitrogen at 2-8 °C.

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References

1. Coleman, R. A.; et al., VIII International Union of Pharmacology classification of prostanoid receptors: properties, distribution, and structure of the receptors and their subtypes**.** Pharm. Rev. **46**, 205-229 (1994).
2. Ocklind, A., et al., Localization of the prostaglandin $F_{2\alpha}$ receptor in rat tissues. Prostaglandins Leukot. Essent. Fatty Acids, **57**, 527—532 (1997).
3. Griffin, B.W., et al., Pharmacological characterization of an FP prostaglandin receptor on rat vascular smooth muscle cells (A7r5) coupled to phosphoinositide turnover and intracellular calcium mobilization. J. Pharmacol. Exp. Ther**., 286**, 411-418 (1998).
4. Sharif, N.A., et al., Pharmacology of [^{3}H]-prostaglandin E_1/[^{3}H]-prostaglandin E_2 and [^{3}H]-prostaglandin $F_{2\alpha}$ binding EP_3 and FP prostaglandin receptor binding sites in bovine corpus luteum: Characterization and correlation with functional data. J. Pharmacol. Exp. Ther. **286**, 1094-1102 (1999).
5. Griffin, B.W., et al., AL–8810: A novel prostaglandin F_2 analog with selective antagonist effects at the prostaglandin F_2 (FP) receptor. J. Pharmacol. Exp. Ther. **290**, 1278-1284 (1999).
6. Sharif, N.A., et al., Bimatoprost and its free acid are prostaglandin FP receptor agonists. Eur. J. Pharmacol., **432,** 211-213 (2001).

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