L-655,240

Product Number L 9539
Store at Room Temperature

Cas #: 103253-15-2
Chemical name: 3-[1-(4-Chlorobenzyl)-5-fluoro-3-methyl-indol-2-yl]-2,2-dimethyl propanoic acid

Product Description
Molecular Formula: C_{21}H_{21}O_{2}NClF
Molecular Weight: 373.85
Appearance: off-white powder
Purity: 98% by HPLC

Thromboxane TP prostanoid (TP) receptors are coupled via regulatory G proteins to stimulate inositol phospholipid (IP) hydrolysis. They are present in all mammalian vascular and airway smooth muscle tissues, in placenta and platelets where they mediate smooth muscle contraction and platelet aggregation and have been implicated in the pathogenesis of myocardial infarction, stroke, and bronchial asthma. Mice deficient in TP prostanoid receptors exhibit prolonged bleeding times and their platelets do not aggregate after exposure to TP prostanoid receptor agonists or to collagen stimulation. Mice genetically deficient in the TP prostanoid receptors or treated with TP prostanoid receptor antagonists have diminished vascular injury responses.

L-655,240 is a selective TP prostanoid receptor antagonist that induces platelet aggregation, contraction of vascular and smooth muscle and increases PI turnover with elevation of intracellular free Ca^{2+}. L-655,240 potently, competitively and selectively inhibits contractions induced in vitro by the TP prostanoid receptor agonist U-44069 in guinea-pig tracheal chain cells (pA_2=8.0), pulmonary artery cells (pA_2=8.4) and thoracic aorta ring (pA_2=8.0). L-655,240 prevents the aggregation of washed human platelets induced by U-44069 with an IC_{50} of 7 nM, as well as aggregation of human platelet rich plasma induced by U-46619, thromboxane A_2 and collagen. It does not inhibit aggregation induced by ADP or platelet activating factor. L-655,240 administered intravenously (i.v.) to guinea pigs prevents bronchoconstriction induced by intravenous injection of U-44069 and arachidonic acid with ED_{50} of 0.09 and 0.23 mg/kg, respectively. Bronchoconstriction induced by histamine, acetylcholine or serotonin is not affected.

Administration of L-655,240 to rats receiving low subcutaneous doses of cyclosporin A for the treatment of refractory autoimmune diseases prevents the negative renal hemodynamic side effects of cyclosporin A, including increased renal vascular resistance, decreased renal blood flow and glomerular filtration rate (GFR).

Dogs pretreated in vivo with L-655,240 exhibit significantly fewer allergen-induced airway contractions, indicating that blockade of TP prostanoid receptors by L-655,240 and subsequent increase in intracellular calcium levels inhibits late allergen responses of bronchial tissues.

Preparation Instructions
L-655,240 is soluble in DMSO at 30 mg/mL and insoluble in water (<2 mg/mL).

Storage/Stability
Store tightly sealed at room temperature.

References
