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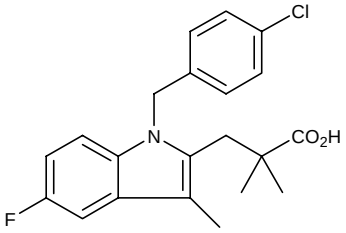
# ProductInformation

**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: $C_{21}H_{21}O_2NClF$
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 insitol 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.[1] 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.[2] Mice genetically deficient in theTP prostanoid receptors or treated with TP prostanoid receptor antagonists have diminished vascular injury responses.[3]

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).[4] 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.[4]
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 $mg/kg^{-1}$ respectively.[4] 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).[5]

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.[6]

**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**
1. Hirata, T., et al., Two thromboxane $A_2$ receptor isoforms in human platelets: opposite coupling to adenylyl cyclase with different sensitivity to arg60-to-leu mutation. J. Clin. Invest., **97**, 949-956, (1996).
2. Thomas, D. W., et al., Coagulation defects and altered hemodynamic responses in mice lacking receptors for thromboxane $A_2$. J. Clin. Invest., **102,** 1994-2001 (1998).
3. Cheng, W., et al., Role of prostacyclin in the cardiovascular response to thromboxane $A_2$. Science, **296**, 539-541 (2002).

4. Hall, R. A., et al., Pharmacology of L-655,240 (3-[1-(4-chlorobenzyl)-5-fluoro-3-methyl-indol-2-yl]2,2-dimethylpro pan oic acid); a potent, selective thromboxane/prostaglandin endoperoxide antagonist. Eur. J. Pharmacol., **135**,193-201 (1987).
5. Bunke, M., et al., Protection of glomerular filtration rate by the thromboxane receptor antagonist L-655,240 during low dose cyclosporine administration. Prostaglandins, **43**, 351-360 (1992).
6. Janssen, L.J., et al., Myogenic and neurogenic mechanisms and arachidonate metabolites in bronchial muscle response to allergen. Am. J. Physiol., **273**, L1118-L1125 (1997).

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