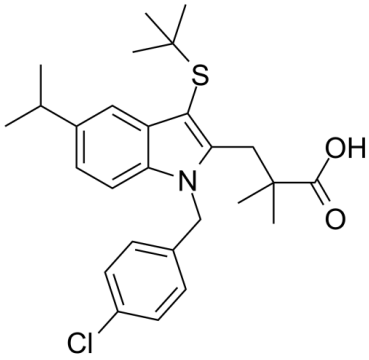
Data Sheet

Product Name:	MK-886
Cat. No.:	CS-5755
CAS No.:	118414-82-7
Molecular Formula:	$C_{27}H_{34}ClNO_2S$
Molecular Weight:	472.08
Target:	Apoptosis; FLAP; Leukotriene Receptor; PPAR
Pathway:	Apoptosis; Cell Cycle/DNA Damage; GPCR/G Protein; Immunology/Inflammation
Solubility:	DMSO : 75 mg/mL (158.87 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

MK-886 (L 663536) is a potent, cell-permeable and orally active **FLAP** (**IC_{50}** of 30 nM) and **leukotriene biosynthesis** (**IC_{50}**s of 3 nM and 1.1 μM in intact leukocytes and human whole blood, respectively) inhibitor. MK-886 is also a non-competitive **PPARα** antagonist and can induce **apoptosis**[1][2][3]. IC50 & Target: IC50: 30 nM (FLAP)[3]

IC50: 3 nM (Leukotriene biosynthesis in intact leukocytes) and 1.1 μM (Leukotriene biosynthesis in human whole blood)[2]

PPARα[1] **In Vitro:** MK-886 (0.5-2 μM; 15 hours; primary keratinocytes) treatment reduces keratin-1 expression in a culture of mouse primary keratinocytes[1].

Using a transient transfection system in monkey kidney fibroblast CV-1 cells, mouse keratinocyte 308 cells and human lung adenocarcinoma A549 cells, 10 μM MK-886 is able to inhibit Wy-14643 activation of PPARα by ~80%. MK-886 also decreases PPAR α activation by fatty acids in the stable transfection system[1].

Although Jurkat cells express all PPAR isoforms, various PPARα and PPARγ agonists are unable to prevent MK-886-induced apoptosis[1]. **In Vivo:** MK-886 (L 663536; 5 mg/kg; oral administration; male Sprague-Dawley rats) treatment potently inhibits the antigen-induced dyspnea in inbred rats pretreated with methysergide[2].

MK-886 (L 663536) inhibits leukotriene biosynthesis in vivo in a rat pleurisy model (ED_{50}, 0.2 mg/kg p.o.), an inflamed rat paw model (ED_{50}, 0.8 mg/kg), a model of leukotriene excretion in rat bile following antigen provocation[2].

References:

[1]. [1] Kehrer JP et al. Inhibition of peroxisome-proliferator-activated receptor (PPAR)alpha by MK886. Biochem J. 2001 Jun 15.

[2]. [2] Gillard J et al. L-663,536 (MK-886) (3-[1-(4-chlorobenzyl)-3-t-butyl-thio-5-isopropylindol-2-yl]-2,2 - dimethylpropanoic acid), a novel, orally active leukotriene biosynthesis inhibitor. Can J Physiol Pharmacol. 1989 May;67(5):456-64.

[3]. Mancini JA, et al. 5-Lipoxygenase-activating protein is the target of a novel hybrid of two classes of leukotriene biosynthesis inhibitors. Mol Pharmacol. 1992 Feb;41(2):267-72.

CAIndexNames:

1H-Indole-2-propanoic acid, 1-[(4-chlorophenyl)methyl]-3-[(1,1-dimethylethyl)thio]-α,α-dimethyl-5-(1-methylethyl)-

SMILES:

CC(C)C1=CC=C(N(CC2=CC=C(Cl)C=C2)C(CC(C)(C(O)=O)C)=C3SC(C)(C)C)C3=C1

Caution: Product has not been fully validated for medical applications. For research use only.

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