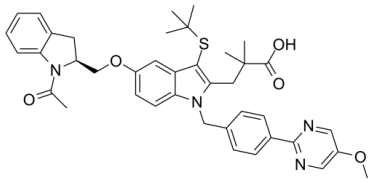
Data Sheet

Product Name:	AM679
Cat. No.:	CS-0935
CAS No.:	1206880-66-1
Molecular Formula:	C40H44N4O5S
Molecular Weight:	692.87
Target:	FLAP
Pathway:	Immunology/Inflammation
Solubility:	H2O : < 0.1 mg/mL (insoluble); DMSO : ≥ 100 mg/mL (144.33 mM)



BIOLOGICAL ACTIVITY:

AM679 is a potent and selective FLAP inhibitor with IC50s of 2.2 nM/0.6 nM/154 nM for FLAP binding/hLA/hWB respectively. IC50 value: 2.2 nM/0.6 nM/154 nM(FLAP binding/hLA/hWB) [1] Target: FLAP in vitro: AM679 showed excellent in vitro inhibition against FLAP. AM679 has an excellent hWB IC50 potency of 154 nM. AM679 showed an improved CYP inhibition profile (IC50 3A4 = 16.7 lM, 2C9 = 3.7 lM, 2D6 >30 lM), no time dependent inhibition against CYP3A4 (0.003 min-1 vs 0.057 min-1 for troleandomycin control 10 uM) and no CYP3A4 induction. in vivo: AM679 was profiled in a rodent bronchoalveolar lavage (BAL) model to measure its ability to inhibit production of leukotrienes in vivo.16 Oral administration of 39 (10 mg/kg as the sodium carboxylate salt) 4 h prior to ionophore challenge reduced LTB4 and CysLT levels in the rodent lung lavage fluid by 98% and 87%, respectively, with corresponding average rodent plasma levels of 605 nM (3 h post dose, rat blood LTB4 IC50 = 125 nM).

PROTOCOL (Extracted from published papers and Only for reference)

Animal administration [2] Female BALB/c mice, 6 to 8 weeks old, are anesthetized by intraperitoneal injection of pentobarbital (50 mg/kg body weight), and virus in 2 µl PBS is dropped into the corneal surface and massaged in with closed eyelids. In each mouse only one eye is treated. The day of the inoculation is considered day 0. AM679 is diluted in PBS to 60 ng/2 µl just prior to topical application of 2 µl (volume) 40 min after the RSV inoculation on day 0 and then each day thereafter for 14 days. This concentration of AM679 in the eye is predicted to give complete LT inhibition but, given the 1,000-fold selectivity determined above, is unlikely to cross over to similar protein targets, such as the cyclooxygenases. At days 0, 2, 4, 6, 8, 10, and 14, three mice from the control group and three mice from the FLAP inhibitor-treated group are sacrificed for ocular disease evaluation and eye and lung tissue preparation for assays.

References:

[1]. Stock, N, et al. 5-Lipoxygenase-activating protein inhibitors. Part 2: 3-<5-((S)-1-Acetyl-2,3-dihydro-1H-indol-2-ylmethoxy)-3-tert-butylsulfanyl-1-[4-(5-methoxy-pyrimidin-2-yl)-benzyl]-1H-indol-2-yl>-2,2-dimethyl-propionic acid (AM679)-A potent FLAP inhibitor. Bioorganic & Medicinal Chemistry Letters (2010), 20(1), 213-217.

[2]. Musiyenko, A, et al. A novel 5-lipoxygenase-activating protein inhibitor, AM679, reduces inflammation in the respiratory syncytial virus-infected mouse eye. Clinical and Vaccine Immunology (2009), 16(11), 1654-1659.

CAIndexNames:

1H-Indole-2-propanoic acid, 5-[[(2S)-1-acetyl-2,3-dihydro-1H-indol-2-yl]methoxy]-3-[(1,1-dimethylethyl)thio]-1-[[4-(5-methoxy-2-

pyrimidinyl)phenyl]methyl]- , -dimethyl-

SMILES:

O=C(C)N1C2=CC=CC=C2C[C@H]1COC3=CC=C(N(CC4=CC=C(C5=NC=C(OC)C=N5)C=C4)C(CC(C)(C(O)=O)C)=C6SC(C)(C)C6=C3

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

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