Product Data Sheet

Product Name: YM158 free base (YM-57158)
Cat. No.: GC31980

Chemical Properties

Cas. No.	179102-65-9		
SMILES	O=C(NC1=CC(CCCS(=O)(C2=CC=C(Cl)C=C2)=O)=CC=C1OCC3=NN=NN3)C4=CC=CC(OCC5=NC(C(C)(C)C)=CS5)=C4		
Formula	$C_{32}H_{33}ClN_6O_5S_2$	M.Wt	681.22
Solubility	Soluble in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	YM158 free base (YM-57158)		

Protocol

Animal experiment:

Guinea pigs[2]Male Hartley guinea pigs are used. Effects of YM158 (30 mg/kg, p.o.) , Pranlukast, and Daltroban are measured on the shortening of onset time for asthmatic response. Each compound is administered p.o. to animals without or with 5 mg/kg or 1 mg/kg of Indomethacin[2].

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

References:

[1]. Arakida Y, et al. In vitro pharmacologic profile of YM158, a new dual antagonist for LTD4 and TXA2 receptors. J Pharmacol Exp Ther. 1998 Nov;287(2):633-9.
[2]. Arakida Y, et al. Effects of lipid mediator antagonists on predominant mediator-controlled asthmatic reactions in passively sensitized guinea pigs. J Pharmacol Exp Ther. 1999 Sep;290(3):1285-91.

Background

YM158 free base is a potent and selective LTD4 and TXA2 receptor antagonist with pA2 values of about 8.87 and 8.81, respectively.

YM158 antagonizes leukotriene (LT) D4 and thromboxane (TX) A2 receptors. Functional assays in vitro show that YM158 exhibits competitive dual antagonism of LTD4 and TXA2 receptor-mediated contraction of isolated guinea pig tracheae, with pA2 values of about 8.87 and 8.81, respectively. Its antagonistic activity for the LTD4 receptor is approximately 6.5 times less potent than that of Montelukast, and that for the TXA2 receptor is 2.5 times more potent than that of Seratrodast. YM158 also inhibits PGD2- and PGF2α -induced tracheal contractions. YM158 antagonizes the stable TXA2 analog U46619-induced aggregation of both guinea pig and human platelets and inhibits the LTD4-induced contraction of guinea pig ileum. YM158 produces a concentration-dependent inhibition of guinea pig ileum contraction induced by 1 nM LTD4 with an IC50 value of 0.58 nM[1].

YM158, an orally active dual antagonist for LTD4 and TXA2 receptors, is expected to have a stronger antiasthmatic efficacy in a broader class of asthmatic patients than single antagonistic drugs.The effect of YM158 is examined on these asthmatic responses in mediator-controlled and passively sensitized guinea pigs. Because the inhibitory

effects of YM158 on increase in the airway resistance induced by LTD4 or U46619 are shown to be dose-dependent when p.o. administered 1 h before LTD4 or U46619 injection, with ED50 values of 8.6 and 14 mg/kg, respectively, the antagonistic activities of p.o. YM158 for LTD4 and TXA2 receptors are exhibited at the same dose range. Oral YM158 shows significant effects, approximately the same as the combination of Pranlukast and Daltroban on antigen-induced response under various conditions; namely, where LTD4 is predominant, TXA2 is predominant; or where both mediators participated equally. In groups not treated with Indomethacin, administration of Daltroban (10 mg/kg), a combination of Pranlukast (30 mg/kg) and Daltroban (10 mg/kg), or YM158 (30 mg/kg) significantly prolongs the onset time for asthmatic response and significantly suppresses symptoms[2].

[1]. Arakida Y, et al. In vitro pharmacologic profile of YM158, a new dual antagonist for LTD4 and TXA2 receptors. J Pharmacol Exp Ther. 1998 Nov;287(2):633-9. [2]. Arakida Y, et al. Effects of lipid mediator antagonists on predominant mediator-controlled asthmatic reactions in passively sensitized guinea pigs. J Pharmacol Exp Ther. 1999 Sep;290(3):1285-91.