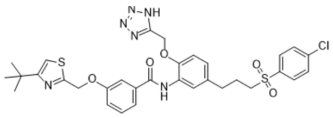
YM158 free base

Cat. No.:	HY-U00355
CAS No.:	179102-65-9
Molecular Formula:	$C_{32}H_{33}ClN_6O_5S_2$
Molecular Weight:	681.22
Target:	Leukotriene Receptor; Prostaglandin Receptor
Pathway:	GPCR/G Protein
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	YM158 free base is a potent and selective LTD_4 and TXA_2 receptor antagonist with pA_2 values of about 8.87 and 8.81, respectively.
IC_{50} & Target	LTD_4 8.87 (pA2) | TXA_2 Receptor 8.81 (pA2)
In Vitro	YM158 antagonizes leukotriene (LT) D_4 and thromboxane (TX) A_2 receptors. Functional assays in vitro show that YM158 exhibits competitive dual antagonism of LTD_4 and TXA_2 receptor-mediated contraction of isolated guinea pig tracheae, with pA_2 values of about 8.87 and 8.81, respectively. Its antagonistic activity for the LTD_4 receptor is approximately 6.5 times less potent than that of Montelukast, and that for the TXA_2 receptor is 2.5 times more potent than that of Seratrodast. YM158 also inhibits PGD_2- and $PGF_{2\alpha}$ -induced tracheal contractions. YM158 antagonizes the stable TXA_2 analog U46619-induced aggregation of both guinea pig and human platelets and inhibits the LTD_4-induced contraction of guinea pig ileum. YM158 produces a concentration-dependent inhibition of guinea pig ileum contraction induced by 1 nM LTD_4 with an IC_{50} value of 0.58 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	YM158, an orally active dual antagonist for LTD_4 and TXA_2 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 LTD_4 or U46619 are shown to be dose-dependent when p.o. administered 1 h before LTD 4 or U46619 injection, with ED_{50} values of 8.6 and 14 mg/kg, respectively, the antagonistic activities of p.o. YM158 for LTD_4 and TXA_2 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 LTD_4 is predominant, TXA_2 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal	Guinea pigs[2]

Administration [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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Arakida Y, et al. In vitro pharmacologic profile of YM158, a new dual antagonist for LTD_4 and TXA_2 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.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA