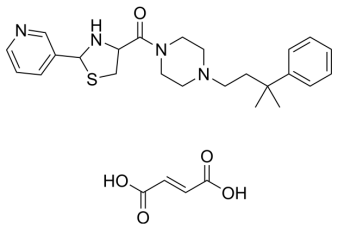
YM-264

Cat. No.:	HY-101833
CAS No.:	131888-54-5
Molecular Formula:	$C_{28}H_{36}N_4O_5S$
Molecular Weight:	540.67
Target:	Platelet-activating Factor Receptor (PAFR)
Pathway:	GPCR/G Protein
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	YM-264 is a selective, potent and orally active platelet-activating factor (PAF) antagonist with a pKi value of 8.85 for rabbit platelet membranes.
IC_{50} & Target	pKi: 8.85 (PAF, rabbit platelet membranes)[1].
In Vitro	The anti-platelet-activating factor effect of YM-264 is examined in vitro. YM-264 inhibits [^{3}H] platelet-activating factor binding to rabbit platelet membranes with a pK_ivalue of 8.85. YM-264 inhibits the platelet-activating factor-induced human, rabbit and guinea-pig platelet aggregation with pA2 values of 8.68, 8.33 and 8.14, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	There are no significant differences in baseline airway responsiveness between control and YM-264 treated groups. Airway hyperresponsiveness induced by antigen exposure is significantly inhibited by the administration of YM-264. The baseline Rrs is 0.40 (0.02) cm H_2O/mL/s in the control group (n=6). In the YM-264 treated groups, the baseline Rrs is 0.39 (0.01) and 0.36 (0.01) cm H_2O/mL/s at a doses of 1 mg/kg (n=5) and 3 mg/kg (n=6), respectively. The Rrs during the IAR significantly increase from baseline to 0.92 (0.10) cm H_2O/mL/s in control (p=0.0002), 0.81 (0.12) in YM-264 1 mg/kg (p=0.01), and 1.06 (0.29) in YM-264 3 mg/kg (p=0.048). Reelevation of Rrs in the late phase is observed in the control group after antigen challenge. At this phase, Rrs significantly increase to 0.72 (0.10) cm H_2O/mL/s (p=0.0101) from the baseline (0.40) at 6 h after the exposure of antigen. In contrast, YM-264 at the doses of 1 and 3 mg/kg show significant inhibition of reelevation of Rrs as compared with control. YM-264 inhibit the eosinophil infiltration dose dependently[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Guine Pigs[2] Male Hartley guinea pigs weighing approximately 300 g are sensitized. The animals are fixed in position with the nose and mouth directed toward the center of the cylinder. Ovalbumin (10 mg/mL) is administered daily for 10 min. On the ninth or tenth day, all of the animals exhibit asthmatic symptoms. Two booster inhalations of AO (10 mg/mL) are subsequently given to the guinea pigs for 5 min at weekly intervals. Forty-five animals are randomized into three experimental groups by the order of their capture from shipping crate. Each group is further divided into three subgroups for control, YM-264 (1 mg/kg) and YM-264 (3 mg/kg). One week after the second booster inhalation, 16 animals for AH experiment are randomly divided into three subgroups for control and YM-264 treatment (1 and 3 mg/kg), and they are exposed to aerosolized OA (10 mg/mL)

for 5 min. A dose of 1 or 3 mg/kg of YM264 is administered orally 30 min before and again, 3 h after the exposure to OA. The control group receives 0.5% methylcellulose in the same volume as YM-264[2].

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

REFERENCES

[1]. Yamada T, et al. Pharmacological properties of YM264, a potent and orally active antagonist of platelet-activating factor. Arch Int Pharmacodyn Ther. 1990 Nov-Dec;308:123-36.

[2]. Arima M, et al. Effect of YM264 on the airway hyperresponsiveness and the late asthmatic response in a guinea pig model of asthma. Chest. 1995 Aug;108(2):529-34.

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