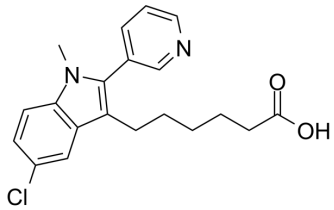
CGS 15435

Cat. No.:	HY-100283
CAS No.:	95853-92-2
Molecular Formula:	$C_{20}H_{21}ClN_2O_2$
Molecular Weight:	356.85
Target:	Others
Pathway:	Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	CGS 15435, a potent thromboxane (TxA_2) synthetase inhibitor with an IC_{50} of 1 nM, has a selectivity for Tx synthetase 100000-fold greater than that for cyclooxygenase, PGI_2 synthetase and lipoxygenase enzymes.
IC_{50} & Target	TXA_2 1 nM (IC_{50})
In Vitro	CGS 15435 is a highly specific Tx synthetase inhibitor. CGS 15435 is only weakly effective as an inhibitor of PGE_2 (Cyclooxygenase, IC_{50}=1200 μM), prostacyclin (PGI_2 synthetase, IC_{50}=90 μM) or 5-Lipoxygenase (IC_{50}=60 μM) product formation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	CGS 15435 has a long duration of action, since the increases in the plasma levels of TxB_2 are prevented even at 24 h after CGS 15435 administration. CGS 15435 significantly inhibits TxB_2 formation 4, 6, 12 and 24 h after dosing. Administration of CGS 15435 0.25 or 24 h prior to Arachidonic acid (AA) produced no increase in TxB_2 in the surviving animals (4/4 and 5/6, respectively). The final TxB_2 levels in the CGS15435A (0.25 and 24 h pretreatment) groups are significantly lower ($P<0.05$) than those seen in the AA or the Dazoxiben (2 h pretreatment) groups[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Thromboxane synthetase, cyclooxygenase, prostacyclin synthetase, and lipoxygenase enzymes are prepared. For the individual enzyme assays. [1-^{14}C]Arachidonic acid (AA) is incubated with partially purified enzyme obtained from human platelets (thromboxane synthetase), sheep seminal vesicles (cyclooxygenase), bovine aorta (prostacyclin synthetase), and guinea-pig leukocytes (lipoxygenase). At the end of the incubation period, the products are extracted into ethyl acetate, the extracts are evaporated to dryness, the residues are redissolved in acetone, and these solutions are spotted on thin layer chromatography plates. The plates are developed in the appropriate solvents, scanned and radioactive spots corresponding to those of TxB_2, PGE_2, 6-keto PGFu, and 5-HETE, are scraped off and counted by a radiospectrometer. The IC_{50} values are determined by employing a range of concentrations of test compounds over the linear range of the assay and analyzed graphically. All determinations are done in duplicate and repeated once[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration [1]	Rabbits[1] Adult male New Zealand rabbits (2.3-3.5 kg) are anesthetized with sodium pentobarbital (30 mg/kg i.v.). The animals are tracheotomized and the left femoral artery and vein are cannulated for the recording of mean arterial blood pressure (MABP) and the injection of either vehicle or drug, respectively. The animals are allowed to stabilize for at least 15 rain prior to drug or vehicle administration. CGS 15435 and DAZ are dissolved in 2 mL of 0.5 M Tris buffer (pH 8.4) and injected i.v. over a 15 s period. CGS 15435 (8.6 μmol/kg; 3.1 mg/kg) is administered at 15 min (n=4) or 24 h (n=6) prior to AA. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Olson RW, et al. CGS 15435A, a thromboxane synthetase inhibitor with an extended duration of action: a comparison with dazoxiben. Eur J Pharmacol. 1987 Jan 20;133(3):265-73.

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