ZD-1611

Cat. No.: HY-19274

CAS No.: 186497-38-1

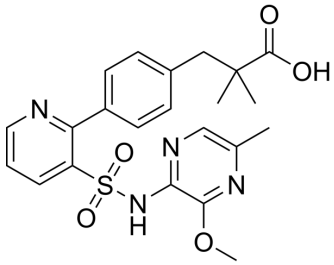
Molecular Formula: $C_{22}H_{24}N_4O_5S$

Molecular Weight: 456.51

Target: Endothelin Receptor

Pathway: GPCR/G Protein

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	ZD-1611 is a potent, orally active, selective ETA receptor antagonist, used for the research of ischemic stroke.
IC_{50} & Target	ET_A
In Vitro	ZD1611 competitively inhibits ^{125}I-labeled ET-1 binding at human cloned ETA and ETB receptors with pIC_{50} values of 8.6 and 5.6, respectively, showing 1000-fold selectivity for the ETA receptor[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ZD1611 (0.3 mg/kg, p.o.) has a duration of action of more than 7 h in rats. In the dog, ZD1611 is active for at least 6 h at dose of 0.6 mg/kg p.o[1]. ZD1611 (0.15 mg/kg/day) in combination with candesartan decreases the brain damage and improves the neurological scores in rats. However, ZD1611 or candesartan alone does not significantly decrease the brain damage or improve neurological scores[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	The precursor of ET-1, big ET-1, is used for in vivo analysis of the effects of ZD1611. Exogenously administered big ET-1 is converted to the biologically active peptide ET-1 in vivo via a phosphoramidon-sensitive ET-converting enzyme. In the present study, the use of big ET-1 in vivo is preferred because this compound fails to elicit the initial depressor response associated with i.v. administered ET-1 and yields a greater maximum response than that to ET-1 itself. A partial cumulative dose-response curve to i.v. big ET-1 starting at 0.3 nmol/kg) is constructed until pressor responses >30 mm Hg are achieved. After a 55-min recovery period, ZD1611 (0.03-0.3 mg/kg) or vehicle is administered, and the big ET-1-response curve is repeated 5 min later. The activity of ZD1611 is calculated as a ratio of the dose of big ET-1 required to give a 30-mm Hg rise in MAP in the absence and then the presence of the compound. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Wilson C, et al. Pharmacological profile of ZD1611, a novel, orally active endothelin ETA receptor antagonist. J Pharmacol Exp Ther. 1999 Sep;290(3):1085-91.

[2]. Stenman E, et al. Cooperative effect of angiotensin AT(1) and endothelin ET(A) receptor antagonism limits the brain damage after ischemic stroke in rat. Eur J Pharmacol. 2007 Sep 10;570(1-3):142-8. Epub 2007 Jun 9.

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