Bioactive Molecules, Building Blocks, Intermediates
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Data Sheet

Product Name: Ambrisentan  
Cat. No.: CS-0447  
CAS No.: 177036-94-1  
Molecular Formula: C_{22}H_{22}N_{2}O_{4}  
Molecular Weight: 378.42  
Target: Endothelin Receptor  
Pathway: GPCR/G Protein  
Solubility: DMSO : ≥ 76 mg/mL (200.84 mM); Ethanol : 38 mg/mL (100.42 mM; Need ultrasonic)

BIOLOGICAL ACTIVITY:
Ambrisentan is a selective ET type A receptor (ETAR) antagonist.
IC50 & Target: ETA receptor

**In Vitro:** Ambrisentan is an endothelin type A receptor antagonist. Ambrisentan induces Nrf2 activation. Endothelial permeability increased in BMEC monolayers at 24 h of hypoxia exposure and compared to vehicle control, Ambrisentan attenuates hypoxia-induced BMEC leak. These results are reversed when prior to treatment BMEC are transfected with siRNA against Nrf2.

**In Vivo:** In the Ambrisentan group, hepatic hydroxyproline content is significantly lower than in the control group (18.0 μg/g±6.1 μg/g vs 33.9 μg/g±13.5 μg/g liver, respectively, P=0.014). Hepatic fibrosis estimated by Sirius red staining and areas positive for α-smooth muscle actin, indicative of activated hepatic stellate cells, are also significantly lower in the Ambrisentan group (0.46%±0.18% vs 1.11%±0.28%, respectively, P=0.0003; and 0.12%±0.08% vs 0.25%±0.11%, respectively, P=0.047). Moreover, hepatic RNA expression levels of procollagen-1 and tissue inhibitor of metalloproteinase-1 (TIMP-1) are significantly lower by 60% and 45%, respectively, in the Ambrisentan group. Inflammation, steatosis, and endothelin-related mRNA expression in the liver are not significantly different between the groups. Ambrisentan attenuates the progression of hepatic fibrosis by inhibiting hepatic stellate cell activation and reducing procollagen-1 and TIMP-1 gene expression. Ambrisentan did not affect inflammation or steatosis.

PROTOCOL (Extracted from published papers and Only for reference)

**Cell Assay:** Ambrisentan is dissolved in DMSO and stored, and then diluted with appropriate medium before use. Unless otherwise stated, for each BMEC experiment cells are randomly divided into 4 groups: (1) normoxia vehicle control (Nx-CTRL); (2) normoxia-treated; (3) hypoxia (24 h) control (Hx-CTRL) and (4) hypoxia (24 h) treated. As previously described, Nrf2 activators are added 24 h prior to any hypoxic exposures. Cell treatments are; Protandim (100 μg/mL), methazolamide (125 μg/mL, nifedipine (7 μg/mL) or Ambrisentan (40 μg/mL). In addition, some cells are treated with Nrf2 siRNA. In these experiments, siRNA is added 24 h prior to drug treatments. The rationale for 24 h hypoxia exposure for BMEC is to ensure that cells remained transfected with siRNA for the pre-treatment of drugs (24 h in normoxia) and during the 24 h hypoxia exposure. Data is collected from at least three separate cell culture preparations on three separate days (n=9).

**Animal Administration:** Mice
A total of 13 male FLS-ob/ob mice (age, 8 wk; body weight, 42.88 g±1.74 g) are used. At the age of 12 wk, male FLS-ob/ob mice are randomly assigned to the Ambrisentan (n=8) or control (n= 5) group. Intragastric gavage administration is carried out in conscious animals with an appropriately sized gastric tube. Ambrisentan (2.5 mg/kg per day) is orally administered every afternoon for 4 wk as a bolus through a gastric tube. Water is administered to the control group. At week 4, animals are fasted for 4 h and tail vein blood is drawn and subjected to blood glucose determination. Animals are killed by pentobarbital anesthesia injection after 4 wk and blood is collected from the right ventricle. Plasma samples are frozen and stored at -80°C Liver and visceral fat are then weighed, snap-frozen.

[1] Ambrisentan, product information from ChemScene
[2] Ambrisentan, protocol information from published papers
in liquid nitrogen, and stored at -80°C. Additional liver specimens are fixed in 10% buffered formalin and embedded in paraffin for histological analysis.

References:


Caution: Product has not been fully validated for medical applications. For research use only.

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