# A-192621

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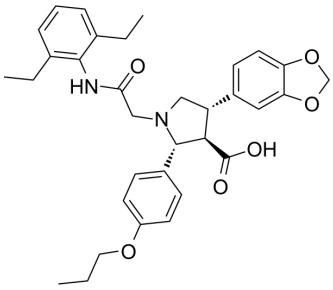
| **Cat. No.:** | HY-120295 |
| **CAS No.:** | 195529-54-5 |
| **Molecular Formula:** | $C_{33}H_{38}N_2O_6$ |
| **Molecular Weight:** | 558.66 |
| **Target:** | Endothelin Receptor; Apoptosis |
| **Pathway:** | GPCR/G Protein; Apoptosis |
| **Storage:** | Powder -20°C 3 years<br>4°C 2 years<br>In solvent -80°C 6 months<br>-20°C 1 month |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : ≥ 100 mg/mL (179.00 mM)

* "≥" means soluble, but saturation unknown.

| Preparing Stock Solutions | Concentration / Solvent / Mass | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 1.7900 mL | 8.9500 mL | 17.9000 mL |
| | 5 mM | 0.3580 mL | 1.7900 mL | 3.5800 mL |
| | 10 mM | 0.1790 mL | 0.8950 mL | 1.7900 mL |

Please refer to the solubility information to select the appropriate solvent.

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.47 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

A-192621 is a potent, nonpeptide, orally active and selective endothelin B ($ET_B$) receptor antagonist with an $IC_{50}$ of 4.5 nM and a $K_i$ of 8.8 nM. The selectivity of A-192621 is 636-fold higher than $ET_A$ ($IC_{50}$ of 4280 nM and $K_i$ of 5600 nM). A-192621 promotes apoptosis in PASMCs. A-192621 alos causes elevation of arterial blood pressure and an elevation in the plasma ET-1 level[1][2][3].

| $IC_{50}$ & Target | | | | |
|---|---|---|---|---|
| | $ET_B$ | $ET_B$ | $ET_A$ | $ET_A$ |
| | 4.5 nM ($IC_{50}$) | 8.8 nM (Ki) | 4280 nM ($IC_{50}$) | 5600 nM (Ki) |

**In Vitro**

A-192621 (1-100 μM; 48 hours; PASMCs) treatment markedly reduces the cell viability of PASMCs in a dose-dependent manner[2].

A-192621 (1-100 μM; 48 hours; PASMCs) treatment significantly increases the caspase-3/7 activity and cleaved caspase-3

expression in PASMCs. A-192621 induces apoptosis in a dose-dependent manner and increases the cells' susceptibility to apoptosis by Doxorubicin treatment[2].

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

Cell Viability Assay[2]

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| Cell Line: | Pulmonary arterial smooth muscle cells (PASMCs) with Doxorubicin |
| Concentration: | 1 μM, 10 μM, 50 μM, 100 μM |
| Incubation Time: | 72 hours |
| Result: | The viability of PASMCs was significantly decreased in a dose-dependent manner. |

Western Blot Analysis[2]

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|---|---|
| Cell Line: | Pulmonary arterial smooth muscle cells (PASMCs) with Doxorubicin |
| Concentration: | 1 μM, 10 μM, 100 μM |
| Incubation Time: | 72 hours |
| Result: | The caspase-3/7 activity in PASMCs was significantly increased in a dose-dependent manner. |

**In Vivo**

A-192621 (30-100 mg/kg; oral administration; daily; for 3 days; male Sprague-Dawley rats) treatment inhibits both dilatory and pressor responses induced by S6c mediated by $ET_B$ with an $ED_{50}$ value of 30 mg/kg, and failed to inhibit the ET-1-induced pressor response mediated by $ET_A$. A-192621 alone causes elevation of arterial blood pressure and an elevation in the plasma ET-1 level in the conscious normotensive rat[3].

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

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|---|---|
| Animal Model: | Male Sprague-Dawley rats (250-350 g)[3] |
| Dosage: | 30 mg/kg 100 mg/kg |
| Administration: | Oral administration; daily; for 3 days |
| Result: | Inhibited both dilatory and pressor responses induced by S6c mediated by $ET_B$ with an $ED_{50}$ value of 30 mg/kg. |

## REFERENCES


[1]. Wu-Wong JR, et al. Pharmacology of endothelin receptor antagonists ABT-627, ABT-546, A-182086 and A-192621: in vitro studies. Clin Sci (Lond). 2002 Aug;103 Suppl 48:107S-111S.

[2]. Sakai S, et al. Antagonists to endothelin receptor type B promote apoptosis in human pulmonary arterial smooth muscle cells. Life Sci. 2016 Aug 15;159:116-120.

[3]. Wessale JL, et al. Pharmacology of endothelin receptor antagonists ABT-627, ABT-546, A-182086 and A-192621: ex vivo and in vivo studies. Clin Sci (Lond). 2002 Aug;103 Suppl 48:112S-117S.

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

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