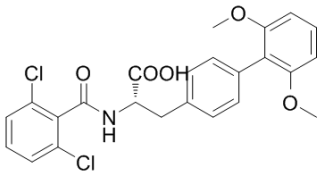
TR-14035

Cat. No.:	HY-15770
CAS No.:	232271-19-1
Molecular Formula:	$C_{24}H_{21}Cl_2NO_5$
Molecular Weight:	474.33
Target:	Integrin
Pathway:	Cytoskeleton
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 41 mg/mL (86.44 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1082 mL	10.5412 mL	21.0824 mL
	5 mM	0.4216 mL	2.1082 mL	4.2165 mL
	10 mM	0.2108 mL	1.0541 mL	2.1082 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 (5.27 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.27 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TR-14035 is a dual $\alpha_4\beta_7/\alpha_{4\beta1}$ integrin antagonist, with IC_{50} s of 7 nM and 87 nM for $\alpha_4\beta_7$ and $\alpha_{4\beta1}$, respectively. TR-14035 can be used for the research of inflammation and autoimmune disease[1][2].

IC_{50} & Target

α4β7	α4β1
7 nM (IC_{50})	87 nM (IC_{50})

In Vitro

TR14035 blocks adhesion of RPMI-8866 cells to MAdCAM-Ig by 100% at 1μM, with an approximate IC_{50} of 0.01μM[2].

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

In Vivo

TR-14035 (3 mg/kg; i.g.) produces a significant decrease of the airways hyper-responsiveness to 5-hydroxytryptamine (5-HT) in an experimental model of allergic asthma in Brown Norway rats[3].

TR-14035 exhibits plasma decreased with half-lives of 0.28 h (3 mg/kg for i.v.) and 0.39 h (10 mg/kg for i.g.), and the oral bioavailability (F) is 17%[4].

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

Animal Model:	Male Brown Norway rats (250-300 g)[3]
Dosage:	3 mg/kg
Administration:	Oral gavage, 1 h before and 3 h after antigen challenge
Result:	Suppressed antigen-induced airway hyper-responsiveness and inflammation.

Animal Model:	Male Sprague-Dawley rats (250-320 g) [4]
Dosage:	3 mg/ kg for i.v.; 10 mg/kg for i.g.
Administration:	Intravenous injection and oral gavage
Result:	$T_{1/2}$ (1.88 h for i.v.; 3.42 h for i.g.), F (17%).

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2019 Dec 17;116(51):25860-25869.
- FASEB J. 2021 Feb;35(2):e21282.
- Obesity. 2015 Apr;23(4):779-85.

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REFERENCES

[1]. Sircar I, et al. Synthesis and SAR of N-benzoyl-L-biphenylalanine derivatives: discovery of TR-14035, a dual alpha(4)beta(7)/alpha(4)beta(1) integrin antagonist. Bioorg Med Chem. 2002 Jun;10(6):2051-66.

[2]. Egger LA, et al. Alpha(4)beta(7)/alpha(4)beta(1) dual integrin antagonists block alpha(4)beta(7)-dependent adhesion under shear flow. J Pharmacol Exp Ther. 2002 Jul;302(1):153-62.

[3]. Julio Cortijo, et al. A small molecule, orally active, α4β1/α4β7 dual antagonist reduces leukocyte infiltration and airway hyper-responsiveness in an experimental model of allergic asthma in Brown Norway rats. Br J Pharmacol. 2006 Mar; 147(6): 661–670.

[4]. M Tsuda-Tsukimoto, et al. Pharmacokinetics and metabolism of TR-14035, a novel antagonist of a4ss1/a4ss7 integrin mediated cell adhesion, in rat and dog. Xenobiotica

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

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