For Research Use Only

TR-14035

proteintech
www.ptgcn.com

Catalog Number: CM04782

产品信息

Catalog Number:
CM04782

CAS号:
232271-19-1

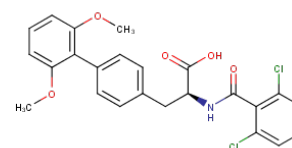
分子式:
$C_{24}H_{21}Cl_2NO_5$

主要靶点:
Integrin

主要通路:
细胞骨架

分子量:
474.33

溶解度:
DMSO:40 mg/mL (84.33 mM);H2O:Insoluble



靶点活性

α4β1 integrin:87 nM| α4β7 integrin:7 nM

体外活性

TR-14035（IC50：alpha(4)beta(7)/alpha(4)beta(1)=7/87 nM）已完成欧洲的第一阶段研究[1]。在大鼠和人类肝细胞中，TR-14035的摄取是通过一个明显的单一饱和机制进行的，其K(m)分别为6.7和2.1 microM，而牛磺胆酸和地高辛可以减少这种摄取。在卵母细胞中表达的OATP1B1/OATP-C 和 OATP1B3/OATP8介导了TR-14035的摄取，其K(m)分别为7.5和5.3 microM[2]。TR14035阻断了人类alpha(4)beta(7)与(125)I-MAdCAM-Ig融合蛋白的结合，IC(50)值为0.75 nM。在体外剪切流条件下，TR14035阻断了表达人类alpha(4)beta(7)的RPMI-8866细胞或小鼠肠系膜淋巴结淋巴细胞与MAdCAM-Ig的结合，IC(50)值为0.1 microM[3]。

体内活性

在EHBRs中，未变化的TR-14035的胆汁排泄和全身清除率显著低于正常大鼠，而在野生型与mdr1a/b-或Bcrp基因敲除小鼠之间，清除率无显著差异[2]。TR14035阻断了对HEVs的粘附(ED50：0.01-0.1 mpk i.v.)[3]。

动物实验

For biliary excretion studies in mice and rats, a cannula (polyethylene tube, SP8 for mice and SP10 for rats) was inserted into the bile duct of the anesthetized animal. In the rat, after complete recovery from diethyl ether anesthesia, TR-14035 was administered intravenously at a dose of 3 mg/ml/kg, and the bile, urine, and blood were collected at designated time intervals. In the mouse, TR-14035 was administered intravenously at a dose of 3 mg/4 ml/kg, and the bile and blood were collected at designated time intervals under pentobarbital anesthesia. Blood was centrifuged to separate plasma, and all the samples were stored at j20 -C until analysis by LC-MSD [2].

细胞实验

RPMI8866 cell line and Jurkat T lymphoblastoid cell line were grown as a suspension culture in RPMI 1640 media, 10% FCS, 2 mM glutamine, 100 units/mL penicillin G, 100 mg/mL streptomycin sulfate at 37 °C and 5% CO2. Adhesion assays have been detailed elsewhere. Microtiter plates were coated with 20 mg/mL HSA for 2 h at room temperature, washed once with PBS and derivatized with 10 mg/mL SPDP for 1 h. After washing, CS-1 (or sCS-1) derived peptide solution (100 mL at 100 μg/mL) was added to the wells and allowed to crosslink to the plates overnight at 4 °C. Non-reacted sites were blocked with 100 mL of 1% OV in PBS for 1 h at 37 °C. RPMI8866 cells were suspended in Dulbecco's modified Eagle's medium with 0.25% OV at a density of 2.5 ×106/mL and incubated for ~1 h at 37 °C with varying concentrations of antagonists on peptide-coated plates. Following washing (EL404 plate washer), bound cells were quantified by measuring endogenous N-acetyl-hexosaminidase activity by reading the optical density at 405 nm using the enzyme substrate p-nitrophenol-N-acetyl-b-d-glucoseaminide. IC50 values were generated by nonlinear regression from titration curves of antagonists from seven doses and reported as the average of a minimum of two experiments. Since experimental variability was noted with respect to the IC50 of the internal standard [(1S - cis) - N - [(3 - carboxy - 2,2,3 - trimethylcyclopentyl)- carbonyl]-O-[(2,6-dichlorophenyl)methyl]-l-tyrosine] a normalization procedure was done using the global mean value [IC50=0.224±0.17 μM (N=19)] of the internal standard. For the Jurkat cell adhesion assay, OV was replaced with 0.25% HSA for both blocking and adhesion buffers. Standard error of the mean for the Jurkat cell adhesion assay was typically <10% for each experiment and no normalization was needed [1].

储存

Powder: -20°C for 3 years | In solvent: -80°C for 1 year | Shipping with blue ice.