For Research Use Only

BMS-378806

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Catalog Number: CM17661

产品信息

Catalog Number:
CM17661

CAS号:
357263-13-9

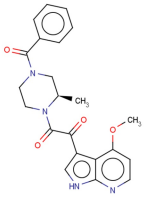
分子式:
$C_{22}H_{22}N_4O_4$

主要靶点:
HIV Protease|gp120/CD4

主要通路:
微生物学|免疫与炎症|蛋白酶体

分子量:
406.43

溶解度:
Ethanol:3 mg/mL (7.38 mM),DMSO:81 mg/mL (199.29 mM),H2O:<1 mg/mL



靶点活性

CD4-gp120 interactions:0.85 nM-26.5 nM(EC50)

体外活性

BMS-806, a 7-azaindole derivative, binds gp120 and interferes with the interaction of HIV surface protein gp120 with the host cell receptor CD4. BMS-806 inhibits a panel of macrophage- and T cell-tropic HIV-1 strains, which are laboratory strains that use either CCR5 (M-tropic) or CXR4 (T-tropic) co-receptors to enter cells and are classified as B subtypes. The aqueous solubility from the crystalline form of BMS-806 (BMS 378806) is 170 μg/mL. The solubility of BMS-806 is 1.3 mg/mL at pH=2.1 and 3.3 mg/mL at pH=11, a solubility profile that reveals the amphoteric nature of BMS-806 and estimates the pKa of the protonated form as 2.9 while that of the free base is approximately 9.6. BMS-806 competes with soluble CD4 binding to a monomeric form of gp120 in an ELISA assay with IC50 = ~ 100 nM. BMS-806 is specific towards HIV-1, with no significant inhibitory activity against HIV-2, SIV, MuLV, RSV, HCMV, BVDV, VSV, and influenza virus observed at concentrations ranging from 10 to 30 μM and no overt cytotoxicity toward host cells, CC50 values > 225 μM. [1] BMS-806 binds directly to gp120 at a stoichiometry of approximately 1:1, with a binding affinity similar to that of soluble CD4. The potential BMS-806 target site is localized to a specific region within the CD4 binding pocket of gp120 by using HIV-1 gp120 variants carrying either compound-selected resistant substitutions or gp120-CD4 contact site mutations. [2]

体内活性

When BMS-806 is administered dose-proportional increases in the AUC and Cmax is observed. In rat, dog and monkey, plasma levels of drug exceeded the concentrations required to half-maximally inhibit virus replication in vitro. The volume of distribution of BMS-806 ranges from 0.4 to 0.6 L/kg, indicative of partitioning beyond plasma; however, examination of brain levels in the rat revealed minimal CNS penetration. [1] BMS-806 is stable in human, rat, dog and monkey blood at 37 °C during a 2-h incubation. The blood-to-plasma concentration ratios in humans, rats, dogs and monkeys are 1.1, 0.77, 1.2 and 0.92 (n=3), respectively, suggesting that BMS-806 is distributed to approximately the same extent between plasma and blood cells. The human clearance of BMS-806 predicted from microsomes is 9.2 ml/min/kg (46% of the hepatic blood flow). [3]

细胞实验

To determine cytotoxicity, MT-2 cells are incubated in the presence of serially diluted BMS-806 for 6 days and cell viability is quantitated using an XTT [2,3-bis(2-methoxy-4-nitro-5-sulfophenyl-2H-tetrazolium-5-carboxanilide] assay to calculate the 50% cytotoxic concentrations (CC50s). (Only for Reference)

描述

BMS-378806 (BMS-806) selectively inhibits the binding of HIV-1 gp120 to the CD4 receptor with EC50 of 0.85-26.5 nM in virus.

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years