For Research Use Only

A-443654

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Catalog Number: CM09772

产品信息

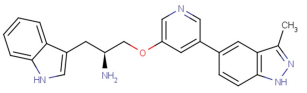
Catalog Number:
CM09772

CAS号:
552325-16-3

分子式:
$C_{24}H_{23}N_5O$

分子量:
397.47

溶解度:
DMSO:100 mg/mL (251.59 mM)



主要靶点:
FLT|GSK-3|Casein Kinase|Akt|CDK|PKC|Chk|Src|MAPK|VEGFR|S6 Kinase|PKA|ERK

主要通路:
表观遗传|细胞骨架|MAPK信号通路|代谢|蛋白酪氨酸激酶|细胞周期|PI3K/Akt/mTOR信号通路|血管生成|干细胞

靶点活性

PKA:6.3 nM (ki)|KDR:3.1 μM (ki)|MAPK-AP2:3.3 μM (ki)|Akt3:160 pM (ki)|PKC δ:33 nM (ki)|PKC γ:24 nM (ki)|CK2:2.4 μM (ki)|Chk1:2.3 μM (ki)|cKIT:1.2 μM (ki)|ERK2:340 nM (ki)|Akt1:160 pM (ki)|GSK3 β:41 nM (ki)|Akt2:160 pM (ki)|RSK2:11 nM (ki)|Src:2.6 μM (ki)|CDK2:24 nM (ki)

体外活性

A-443654 exhibits a Ki of 160 pM which is a 30,000-fold improvement in potency versus the initial lead molecule. A-443654 reduces the P-GSK3 in a dose-responsive manner in all three cell lines. A-443654 is 40-fold selective for Akt over PKA, and it inhibits Akt1, Akt2, or Akt3 equally within cells. A-443654-induced morphological changes occur very rapidly (within 2 to 4 h) in both 10A and 10CA1a cells, with 10CA1a cells more sensitive to A-443654 than the 10A cells. A-443654 inhibits the proliferation of tumor cells with EC50 of 0.1 μM[1]. A-443654 demonstrates the greatest selective effect on the mutant cells compared to the WT cells with greater than 3.5 fold relative growth inhibition of the mutant cells[3]. FACScan Analysis of rapamycin and A-443654 effects on DNA content in 10A and 10CA1a cells. In contrast, A-443654 at 2 and 5 μM decreases Bcl-2 levels by 30 to 40% in the 10CA1a cells at 8h. The combination of rapamycin with 2 or 5 μM A-443654, however, markedly decreases Bcl-2 protein levels by appr 40 to 50% in the 10A cells and by appr 70% in the 10CA1a cells, respectively. A-443654 alone at 2 μM causes the 10CA1a cells, but not the 10A cells, to detach from the plate after 12 h, whereas 1 μM of A-443654 causes 10CA1a cells to detach from the plate after 12 h [2].

体内活性

A-443654 (7.5 mg/kg/d, s.c.) inhibits tumor growth in the 3T3-Akt1 flank tumor model. A-443654 (30 mg/kg, s.c.) caused increased levels of phosphorylated Akt1 in MiaPaCa-2 tumors. A-443654 (50 mg/kg, s.c.) induces apoptosis in 3T3-Akt1 flank tumors [1].

描述

A-443654 is a pan-Akt inhibitor. A-443654 has equal potency against Akt1, Akt2, or Akt3 within cells (Ki=160 pM).

储存

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