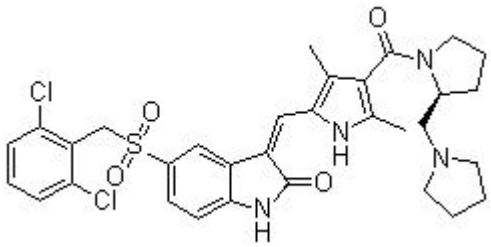
Product Introduction

PHA-665752

PHA-665752 is a potent, selective and ATP-competitive **c-Met** inhibitor with **IC50** of 9 nM, >50-fold selectivity for c-Met than RTKs or STKs.

Technical Data:

Molecular Weight (MW):	641.61	
Formula:	C32H34Cl2N4O4S	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 128 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	477575-56-7	

Biological Activity

PHA-665752 significantly inhibits c-Met kinase activity with Ki of 4 nM, and exhibits >50-fold selectivity for c-Met compared with various tyrosine and serine-threonine kinases. PHA-665752 potently inhibits the HGF-stimulated c-Met autophosphorylation with IC50 of 25-50 nM. PHA-665752 also significantly blocks HGF- and c-Met-dependent functions such as cell motility and cell proliferation with IC50 of 40-50 nM and 18-42 nM, respectively. In addition, PHA-665752 potently inhibits HGF-stimulated or constitutive phosphorylation of mediators of downstream of c-Met such as Gab-1, ERK, Akt, STAT3, PLC-γ, and FAK in

multiple tumor cell lines. [1] PHA-665752 inhibits cell growth in TPR-MET-transformed BaF3 cells with IC50 of <60 nM, and inhibits constitutive cell motility and migration by 92.5% at 0.2 μM. Inhibition of c-Met by PHA665752 (0.2 μM) also induces cell apoptosis of 33.1% and G1 cell cycle arrest with cells in G1 phase increasing from 42.4% to 77.0%. PHA665752 can cooperate with rapamycin to inhibit cell growth of TPR-MET-transformed BaF3 cells and non-small cell lung cancer H441 cells. [2]

Administration of PHA-665752 induces a dose-dependent tumor growth inhibition of S114 xenografts by 20 %, 39% and 68%, at dose of 7.5, 15, and 30 mg/kg/day, respectively. [1] PHA665752 treatment significantly reduces the tumor growth of NCI-H69, NCI-H441 and A549 in mouse xenografts by 99%, 75%, and 59%, respectively. PHA665752 also significantly inhibits angiogenesis by >85%, due to decreasing the production of vascular endothelial growth factor and increasing the production of the angiogenesis inhibitor thrombospondin-1. [3]

References

[1] Christensen JG, et al. Cancer Res, 2003, 63(21), 7345-7355.
[2] Ma PC, et al. Clin Cancer Res, 2005, 11(6), 2312-2319.
[3] Puri N, et al. Cancer Res, 2007, 67(8), 3529-3534.

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