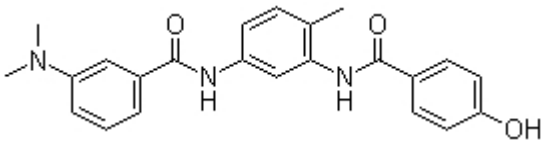
Product Introduction

ZM 336372

ZM 336372 is a potent and selective **c-Raf** inhibitor with **IC50** of 70 nM, 10-fold selectivity over B-RAF, no inhibition to PKA/B/C, AMPK, p70S6, etc.

Technical Data:

Molecular Weight (MW):	389.45	
Formula:	$C_{23}H_{23}N_3O_3$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 78 mg/mL	
	Water <1 mg/mL	
	Ethanol 2 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	208260-29-1	

Biological Activity

ZM 336372 shows 10-fold selectivity over B-Raf. ZM 336372 weakly inhibits SAPK2a/p38α and SAPK2b/p38β with IC50 of 2 μM, and is selective over 17 other protein kinases including PKA, PKC, AMPK, p42 MAPK, MKK1, SAPK1/JNK, and CDK1 even at the concentration of up to 50 μM. ZM 336372 does not prevent constitutive as well as growth factor or phorbol ester induced activation of MKKl or p42 MAPK/ERK2. Moreover, ZM 336372 dose not reverse the phenotype of Ras- or Raf-transformed cell lines. ZM 336372 treatment induces >100 activation of c-Raf and the B-Raf isoform, but it does not trigger any

activation of MKKI or p42 MAPK/ERKP or induce any increase in the GTP-loading of Ras, suggesting that a feedback control loop exists by which Raf isoforms suppress their own activation, such that inhibition is always counterbalanced by reactivation. ZM 336372-induced activation of c-Raf is not prevented by inhibition of the MAPK cascade, protein kinase C or phosphatidylinositide 3-kinase. [1] ZM 336372 (1 μM) abolishes the upregulation of eNOS after treatment with hydrogen peroxide. [2] ZM 336372 treatment in carcinoid tumor cells results in progressive phosphorylation of Raf-1, mitogen-activated protein kinase 1/2, and extracellular signal-regulated kinase 1/2, and causes a significant reduction of bioactive hormone levels as well as the transcription factor, human achaete-scute homologue-1. Furthermore, ZM 336372 treatment leads to a marked suppression of cellular proliferation and induction of the cell cycle inhibitors p21 and p18. [3] ZM 336372 inhibits the proliferation of pheochromocytoma cells, and suppresses NE vasoactive peptide production. [4] ZM 336372 treatment in HepG2 induces the suppression of proliferation in a dose-dependent manner, suppression of hormone secretion, and up-regulation of cell cycle inhibitors. [5] ZM 336372 also induces apoptosis in pancreatic adenocarcinoma cell lines by inhibiting glycogen synthase kinase-3β through phosphorylation of GSK-3β at Ser 9. [6]

References

[1] Hall-Jackson CA, et al. Chem Biol, 1999, 6(8), 559-568.
[2] Wartenberg M, et al. Int J Cancer, 2003, 104(3), 274-282.
[3] Van Gompel JJ, et al. Mol Cancer Ther, 2005, 4(6), 910-917.
[4] Kappes A, et al. J Surg Res, 2006, 133(1), 42-55.
[5] Deming D, et al. J Gastrointest Surg, 2008, 12(5), 852-857.
[6] Deming D, et al. J Surg Res, 2010, 161(1), 28-32.

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