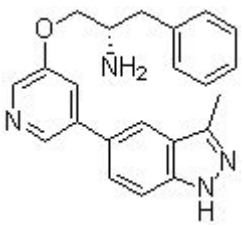
Product Introduction

A-674563

A-674563 is an **Akt1** inhibitor with K_i of 11 nM, modest potent to PKA and >30-fold selective for Akt1 over PKC.

Technical Data:

Molecular Weight (MW):	358.44	
Formula:	$C_{22}H_{22}N_4O$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 72 mg/mL	
	Water 72 mg/mL	
	Ethanol 18 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	552325-73-2	

Biological Activity

A-674563 is achieved from A-443654 by replacing the indole with a phenyl moiety and getting oral activity. A-674563 slows proliferation of tumor cells with EC50 of 0.4 μM. [1] A-674563 does not inhibit Akt phosphorylation per se, but blocks the phosphorylation of Akt downstream targets in a dose-dependent manner. A-674563 induced Akt blockade results in decreased STS cell downstream target phosphorylation and tumor cell growth inhibiton. A-674563 induces G2 cell cycle arrest and apoptosis in STS cells. [2]

20 mg/kg A-674563 increases plasma insulin in an oral glucose tolerance test. A-674563 shows no

significant monotherapy tumor inhibitory activity; the efficacy of the combination therapy is significantly improved compared to paclitaxel monotherapy. [1] A674563-treated (20 mg/kg/bid, p.o.) mice exhibits slower tumor growth and more than 50% decrease in the tumor volume at the termination of the study compared with that in control group. [2] A-674563 is identified to have drastically improved PK profile with oral bioavailability of 67% in mouse, but is 70-fold less active than A-443654. [3] Orally bioavailable compound (achieved by replacing indole of A-443654 with phenyl moiety) and somewhat less selective for Akt over PKA than A-443654.

References

[1] Luo Y, et al, Mol Cancer Ther, 2005, 4(6), 977-986.

[2] Zhu QS, et al, Cancer Res, 2008, 68(8), 2895-2903.

[3] Tatsuya Okuzumi, et al, Mol Biosyst, 2010, 6(8), 1389-1402.

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