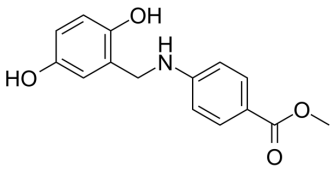
AG957

Cat. No.:	HY-117718
CAS No.:	140674-76-6
Molecular Formula:	$C_{15}H_{15}NO_4$
Molecular Weight:	273.28
Target:	Bcr-Abl
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

AG957 (Tyrphostin AG957;NSC 654705) is a tyrosine kinase inhibitor with anti-BCR/ABL tyrosine kinase activity[1][2]. AG957 is a bcr/abl kinase inhibitor with an IC_{50} of 2.9 μM for $p210^{bcr/abl}$ autokinase activity[3].

In Vitro

AG957 inhibit p210bcr-abl tyrosine kinase activity. AG957 inhibits DNA synthesis as early as 2 h (60% inhibition at 20 microM). AG957 inhibits p210bcr-abl tyrosine phosphorylation in living cells by 1 h without an inhibition of total protein phosphorylation[1].Tyrphostin AG957, a protein tyrosine kinase (PTK) inhibitor which has activity against the $p210^{BCR/ABL}$ kinase, on beta1 integrin function in CML progenitors[2].

AG957 (0.1-100 μM) pretreatment results in significant inhibition of proliferation of chronic myelogenous leukemia (CML) colony-forming cells (CFC) CML CFC[2].

AG957 (25 μM) partially inhibits phosphorylation of several proteins that are BCR/ABL PTK substrates and are involved in normal integrin signaling in BCR/ABL expressing cells[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[2]

Cell Line:	CML and CFC
Concentration:	0, 0.1, 1, 10, 100 μM
Incubation Time:	Pretreatment for 1 hour
Result:	A significant dose-dependent inhibition of CML CFC growth was seen following preincubation with AG957.

Western Blot Analysis[2]

Cell Line:	K562 and BCR/ABL-tranfected M07e cells (MBA-4)
Concentration:	25 μM
Incubation Time:	24 hours
Result:	Partially inhibited tyrosine phosphorylation of p210BCR/ABL, the focal adhesion protein paxillin, the p85 regulatory subunit of the PI3K and the adapter protein cbl in K562 cells. Inhibited phosphorylation of these proteins as well as the adapter protein crkl in MBA4 cells.

In Vivo

AG957 (10 mg/kg; intratracheally 1 h before intratracheal LPS challenge) blocks c-Abl activity in the lung of mice[4].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57BL/6J mice[4]
Dosage:	10 mg/kg
Administration:	Intratracheally 1 h before intratracheal LPS challenge
Result:	LPS induced significant phosphorylation of paxillin at Y31 and Y118. Inhibition of c-Abl by AG957 attenuated LPS-induced phosphorylation of paxillin at both sites. LPS induced significant phosphorylation of VE-cadherin in DMSO-treated mice, which was attenuated in AG957-treated mice.

REFERENCES

[1]. G Kaur, et al. Tyrphostin induced growth inhibition: correlation with effect on p210bcr-abl autokinase activity in K562 chronic myelogenous leukemia. Anticancer Drugs. 1994 Apr;5(2):213-22.

[2]. R Bhatia, et al. Tyrphostin AG957, a tyrosine kinase inhibitor with anti-BCR/ABL tyrosine kinase activity restores beta1 integrin-mediated adhesion and inhibitory signaling in chronic myelogenous leukemia hematopoietic progenitors. Leukemia. 1998 Nov;12(11):1708-17.

[3]. P A Svingen, et al. Effects of the bcr/abl kinase inhibitors AG957 and NSC 680410 on chronic myelogenous leukemia cells in vitro. Clin Cancer Res. 2000 Jan;6(1):237-49.

[4]. Panfeng Fu, et al. c-Abl mediated tyrosine phosphorylation of paxillin regulates LPS-induced endothelial dysfunction and lung injury. Am J Physiol Lung Cell Mol Physiol. 2015 May 15;308(10):L1025-38.

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