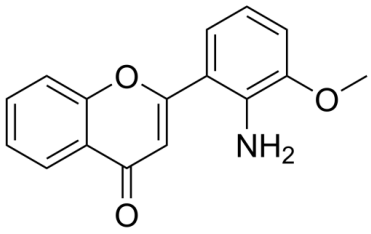
Data Sheet

Product Name:	PD98059
Cat. No.:	CS-0169
CAS No.:	167869-21-8
Molecular Formula:	$C_{16}H_{13}NO_3$
Molecular Weight:	267.28
Target:	Aryl Hydrocarbon Receptor; Autophagy; ERK; MEK
Pathway:	Autophagy; Immunology/Inflammation; MAPK/ERK Pathway; Stem Cell/Wnt
Solubility:	H_2O : < 0.1 mg/mL;DMSO : 33.33 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

PD98059 is a potent and selective **MEK** inhibitor with an **IC_{50}** of 5 μM. PD98059 binds to the inactive form of **MEK**, thereby preventing the activation of **MEK1** (**IC_{50}** of 2-7 μM) and **MEK2** (**IC_{50}** of 50 μM) by upstream kinases. PD98059 is a **ERK1/2** signaling inhibitor. PD98059 is a ligand for the **aryl hydrocarbon receptor (AHR)**, and suppresses TCDD binding (**IC_{50}** of 4 μM) and **AHR** transformation (**IC_{50}** of 1 μM). PD98059 also inhibits ***Mycobacterium bovis*** Bacillus CalmetteGuerin (BCG)-induced **autophagy**[1][2][3].
IC50 & Target:IC50: 2-7 μM (MEK1), 50 μM (MEK2)[1] ***In Vitro:***PD98059 (20 μM; 24 hours) causes G1-phase cell cycle arrest in OCI-AML-3 cells[4].
PD98059 (10 μM; 22 hours) results in concentration-dependent reductions in the dually phosphorylated forms of ERK1 and ERK2[1].
PD98059 both prevents ERK activation and blocks formation of **TDP-43** and HuR-positive SGs[7].
In Vivo:PD98059 (10 mg/kg; i.p.; 1 and 6 hours after Zymosan) significantly reduces the level of p-ERK1/2 in zymosan-injected mice[3]
.

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay:[1]Kinase reactions are performed in 50 μL reaction volumes and contain 50 mM Tris, pH 7.4, 10 mM $MgCl_2$, 2 mM EGTA, 10 μM ATP (containing 1 μCi of 3000 Ci/mmol [γ-^{32}P]ATP), 7.6 μg of GST-MEK1, 7.2 μg of GST-ERK1, and 20 μg of MBP. PD98059 and other flavonoids are added to the reactions mixtures immediately after the addition of GST-MEK1 but before the addition of GST-ERK1 and ATP. Control reactions contain ERK1 and MBP but no MEK. Reaction mixtures are incubated at 30°C for 15 min before being stopped by the addition of Laemmli's SDS sample buffer. Proteins are separated on SDS-15% polyacrylamide gels. After vacuum drying of the gel, radioactivity is detected by autoradiography on X-ray film or phosphoimaging using a BioRad GS-525 Molecular Imager[1]. **Cell Assay:**PD98059 is dissolved in DMSO and stored, and then diluted with appropriate media (DMSO <0.1%) before use[1].[1]The MCF10A, MCF10A-Neo, and MCF10A-NeoT cell lines are used. Subconfluent cultures are treated with PD98059 (0-100 μM). Viability of cells after treatment is assessed by ability to exclude trypan blue. Cultures earmarked for RNA isolation are washed twice with phosphate-buffered saline (2.7 mM KCl, 1.5 mM KH_2PO_4, 137 mM NaCl, 8 mM Na_2HPO_4, pH 7.2) at harvesting and stored at -80°C[1]. **Animal Administration:**PD98059 is prepared in non-pyrogenic saline (0.9% NaCl) (Mice)[3]
.;PD98059 is dissolved in 75% DMSO (Rats)[4].[3][4]Mice[3]
Male CD mice (20-22 g) are randomly allocated into the following groups: 1. Zymosan+DMSO group. Mice are treated intraperitoneally (i.p.) with Zymosan (500 mg/kg, suspended in saline solution) and with the vehicle for PD98059 (10% DMSO, v/v) i.p. 1 and 6 h after Zymosan administration (N=10). 2. PD98059 group. Identical to the Zymosan+DMSO group but are administered PD98059 (10 mg/kg, i.p. bolus) at 1 and 6 h after Zymosan (N=10) instead of DMSO. 3. Sham+DMSO group. Identical to the Zymosan+DMSO group but are administered saline solution instead of Zymosan (N=10). 4. Sham+PD98059 group. Identical to

Sham+DMSO group, except for the administration of PD98059 (10 mg/kg i.p. bolus) 1 and 6 h after saline administration (N=10).
Rats[4]
The rats (male Wistar, 300-350 g) are used. The PD98059 (2.5 μg/5 μL, i.t.) is single or repeated preemptively administered 16 h and 1 h before CCI and then once daily for 7 days. The Vehicle-treated CCI-exposed rats receive 75% DMSO according to the same schedule. There is no significant difference in pain behavior between no-treated and V(DMSO)-treated CCI-exposed rats. This method of PD98059 or vehicle administration is used throughout the study and is referred to in the text as “repeated administration”. At day 7th after CCI 30 min after PD98059 administration tactile allodynia is measured using von Frey test and thermal hyperalgesia is conducted using cold plate test.

References:

[1]. Reiners JJ Jr, et al. PD98059 is an equipotent antagonist of the aryl hydrocarbon receptor and inhibitor of mitogen-activated protein kinase kinase. Mol Pharmacol. 1998 Mar;53(3):438-45.

[2]. Alessi DR, et al. PD 098059 is a specific inhibitor of the activation of mitogen-activated protein kinase kinase in vitro and in vivo. J Biol Chem, 1995, 270(46), 27489-27494.

[3]. Di Paola R, et al. PD98059, a specific MAP kinase inhibitor, attenuates multiple organ dysfunction syndrome/failure (MODS) induced by zymosan in mice. Pharmacol Res. 2010 Feb;61(2):175-87.

[4]. Kojima K, et al. Mitogen-activated protein kinase kinase inhibition enhances nuclear proapoptotic function of p53 in acute myelogenous leukemia cells. Cancer Res. 2007 Apr 1;67(7):3210-9.

[5]. Kim KY, et al. Inhibition of Autophagy Promotes Salinomycin-Induced Apoptosis via Reactive Oxygen Species-Mediated PI3K/AKT/mTOR and ERK/p38 MAPK-Dependent Signaling in Human Prostate Cancer Cells. Int J Mol Sci. 2017 May 18;18(5). pii: E1088.

[6]. Jia Luo, et al. DUSP5 (dual-specificity protein phosphatase 5) suppresses BCG-induced autophagy via ERK 1/2 signaling pathway.

[7]. Sarah J Parker, et al. Inhibition of TDP-43 accumulation by bis(thiosemicarbazonato)-copper complexes. PLoS One. 2012;7(8):e42277.

CAIndexNames:

4H-1-Benzopyran-4-one, 2-(2-amino-3-methoxyphenyl)-

SMILES:

O=C1C=C(OC2=CC=CC=C21)C3=CC=CC(OC)=C3N

Tel: 610-426-3128 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA