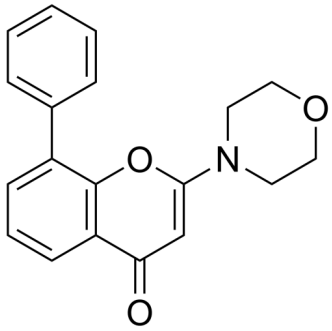
Data Sheet

Product Name:	LY294002
Cat. No.:	CS-0150
CAS No.:	154447-36-6
Molecular Formula:	$C_{19}H_{17}NO_3$
Molecular Weight:	307.34
Target:	Autophagy; PI3K
Pathway:	Autophagy; PI3K/Akt/mTOR
Solubility:	DMSO: 14.9 mg/mL



BIOLOGICAL ACTIVITY:

LY294002 is a broad-spectrum inhibitor of **PI3K**, with **IC_{50}** of 0.5/0.57/0.97 μM for **PI3Kα/PI3Kδ/PI3Kβ**, respectively, also potently inhibits **CK2** with **IC_{50}** of 98 nM.
IC50 & Target: IC50: 0.5/0.57/0.97 μM (PI3Kα/δ/β)[1]
IC50: 98 nM (CK2)[2]
In Vitro: LY294002 (5 μM) completely inhibits the phosphorylation of PKB In HepG2 cells. LY294002 (5 μM) is also shown to block insulin-induced phosphorylation of PKB Ser^{473} in CHO-IR cells[1]. LY294002 is also a potent inhibitor of CK2 (casein kinase 2) with IC_{50} of 98 nM. LY294002 is also able to reduce the kinase activity of both isoforms of the serine/threonine kinases GSK3α and β[2]. When the CNE-2Z cell line is cultured in medium containing LY294002(0 μM, 10 μM, 25 μM, 50 μM, and 75 μM) for 24 h and 48 h, cell proliferation is remarkably decreased in a dose-dependent fashion[3].
In Vivo: Treatment with LY294002 (i.p.,50 mg/kg, 75 mg/kg) significantly reduces mean NPC tumor burden as compared with the control group. Treatment with 10 mg/kg or 25 mg/kg LY294002 is less effective in decreasing tumor burden. Mean NPC tumor burden treated with LY294002 is remarkably decreased in a dose-dependent manner, whereas mean body weight is no obvious difference between control and treated groups (LY294002, 10 mg/kg, 25 mg/kg, 50 mg/kg, and 75 mg/kg)[3].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [2]PI3K inhibition by PI828 and LY294002 is determined in a radiometric assay using purified, recombinant enzymes (class IA and class IB) with 1 μM ATP. The kinase reaction is carried out for 1 h at room temperature (24°C) and is terminated by addition of PBS. IC_{50} values are subsequently determined using a sigmoidal dose-response curve fit (variable slope). CK2 and GSK3β (glycogen synthase kinase 3β) inhibition is established by kinase selectivity screening. Inhibitor (10 μM; PI828 and LY294002) is tested against the Upstate panel of kinases in 10 μM ATP[2]. **Cell Assay:** LY294002 is dissolved in DMSO and stored, and then diluted with appropriate media (DMSO 0.5%) before use[3].[3]Human nasopharyngeal carcinoma cell line CNE-2Z is seeded into 96-well plates at 5000 cells/well. Twenty-four hours after cells are seeded, the medium is removed and replaced in the presence of LY294002 (0 μM, 10 μM, 25 μM, 50 μM, and 75 μM) dissolved in DMSO or DMSO only for an additional 24 h and 48 h. To avoid any nonspecific toxic effects of DMSO on cell growth, DMSO concentrations are maintained at 0.5% in all experiments. MTT dye (5 mg/mL) is added to each well. The reaction is stopped by the addition of DMSO, and optical density is measured at 490 nm on a multiwell plate reader. Background absorbance of the medium in the absence of cells is subtracted. All samples are assayed in triplicate, and the mean for each experiment is calculated. Results are expressed as a percentage of control, which is considered to be 100%[3]. **Animal Administration:** LY294002 is dissolved in vehicle (DMSO).[3][4]Mice[3]
Athymic nude mice are used when they are 6-8 weeks. Mice are randomly divided into free separated into five groups (n=4 mice).

Mice are housed in the same environment with controlled temperature, humidity, and a 12 h light/dark cycle. Mice are inoculated subcutaneously with CNE-2Z cells (1×10^6 cells/mouse in 200 μL of RPMI-1640) into the flank. The tumor take rate is 100%. After 1 week, an intraperitoneal injection is performed to the xenograft mice with different dosage of LY294002 (10 mg/kg, 25 mg/kg, 50 mg/kg, and 75 mg/kg twice weekly (n=4 mice), each group for 4 weeks. Treated mice are monitored any signs. Body weight and tumors size are measured twice a week. Tumor size is measured using calipers and tumor volume is calculated (volume=long axis×short axis^2). At the end of the treatment, all mice are euthanized. One part of tumor tissue is fixed in formalin and embedded in paraffin, and another part is stored at -70°C.

Rats[4]

Male Sprague-Dawley rats weighing 220-240 g are anesthetized by intraperitoneally injecting pentobarbital sodium (50 mg/kg). The animals are divided into 3 groups: NMDA+vehicle (DMSO) (n=46), NMDA+LY294002 (50 nmol) (n=25), and NMDA+Wortmannin (50 nmol) (n=23). Either LY294002 or wortmannin mixed with 200 nmol of NMDA in a total volume of 5 μL is injected into the vitreous cavity of one eye. The same volume of DMSO is injected into the vitreous cavity of the contralateral eye, which is used as a control. The injections are performed under a microscope using a 32-gauge needle, which is connected to a microsyringe. The needle is inserted approximately 1 mm behind the corneal limbus. Damage to neurons and blood vessels in the retina is assessed at 2 and 7 days after the injection. The effects of the intravitreal treatment with either LY294002 or Wortmannin alone on retinal neurons and blood vessels are also examined.

References:

[1]. Chaussade C, et al. Evidence for functional redundancy of class IA PI3K isoforms in insulin signalling. Biochem J. 2007 Jun 15;404(3):449-58.

[2]. Gharbi SI, et al. Exploring the specificity of the PI3K family inhibitor LY294002. Biochem J. 2007 May 15;404(1):15-21.

[3]. Jiang H, et al. Phosphatidylinositol 3-kinase inhibitor(LY294002) induces apoptosis of human nasopharyngeal carcinoma invitro and in vivo. J Exp Clin Cancer Res. 2010 Apr 22;29:34.

[4]. Ueda K, et al. Differential effects of LY294002 and wortmannin on neurons and vascular endothelial cells in the rat retina. Pharmacol Rep. 2013; 65(4):854-62.

[5]. Xiangming Wang, et al. Remote ischemic postconditioning protects against myocardial ischemia-reperfusion injury by inhibition of the RAGE-HMGB1 pathway. Nanjing Medical University. December 2017.

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