

Product Data Sheet

Product Name: QNZ (EVP4593)

Cat. No.: GC11751

Chemical Properties

Cas. No. 545380-34-5

Chemical Name 4-N-[2-(4-phenoxyphenyl)ethyl]quinazoline-4,6-diamine

SMILES C1=CC=C(C=C1)OC2=CC=C(C=C2)CCNC3=NC=NC4=C3C=C(C=C4)N

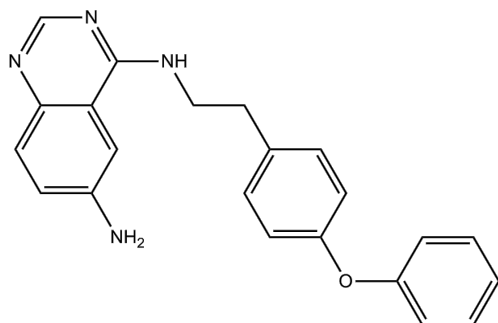
Formula $C_{22}H_{20}N_4O$ M.Wt 356.42

Solubility ≥ 15.05 mg/mL in DMSO, ≥ 10.06 mg/mL in EtOH with ultrasonic Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines Mouse embryonic fibroblast (MEF) cells

Caution: Product has not been fully validated for medical applications. For research use only.

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Cells were treated with a control solvent or 10 μ M QNZ (EVP4593) for 48h, and Preparation Method then cell samples were collected and stained with Ki-67-FITC. Flow cytometry was performed using an Accuri C6-BD to examine Ki-67 expression in MEFs.

Reaction
 Conditions 10 μ M; 48h

Applications QNZ (EVP4593) treatment inhibited the expression of Ki67, a proliferation marker, in fibroblasts.

Animal experiment [2]:

Animal models Sprague Dawley rats

Male Sprague Dawley rats were randomized into eight groups. Rats in the sham group underwent thoracotomy, passing the ligature through the heart but without tying it (150min), and the other seven groups were subjected to 30min of anterior descending coronary artery occlusion followed by 2h of reperfusion and the following treatments: I/R (30min of ischemia and followed by 2h of reperfusion); ischemic postconditioning (IPostC, 30s of ischemia altered with 30s of reperfusion, repeated for three cycles, and followed by reperfusion for 2h); MP (0.3mg/kg morphine administration 10min before reperfusion); MP combined with the HSP90 inhibitor geldanamycin (GA, 1mg/kg); MP combined with the Akt inhibitor GSK-690693 (GSK, 20mg/kg); and MP combined with the C5a inhibitor PMX205 (PMX, 1mg/kg/day, administration via drinking water for 28 days) and MP combined with the NF- κ B inhibitor QNZ (EVP4593) (QNZ, 1mg/kg, i.p.). All inhibitors were administered 10min before morphine and followed by 2h reperfusion.

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Dosage form 1mg/kg; i.p.

Applications QNZ (EVP4593) can enhance MP-induced cardioprotection and alleviate myocardial ischemia/reperfusion injury.

References:

- [1] Huang F, Wang H, Zhang Y, et al. Synergistic effect of QNZ, an inhibitor of NF- κ B signaling, and bone morphogenetic protein 2 on osteogenic differentiation in mesenchymal stem cells through fibroblast-induced yes-associated protein activation[J]. International Journal of Molecular Sciences, 2023, 24(9): 7707.
- [2] Tu R H, Wang D X, Zhong G Q, et al. New targets of morphine postconditioning protection of the myocardium in ischemia/reperfusion injury: Involvement of HSP90/Akt and C5a/NF- κ B[J]. Open Medicine, 2021, 16(1): 1552-1563.

Background

QNZ (EVP4593) is a highly potent and selective inhibitor of the nuclear factor κ B (NF- κ B) signaling pathway with an IC₅₀ value of 11 nM and has anti-inflammatory effects^[1, 2]. QNZ (EVP4593) is a neuroprotective agent that acts by inhibiting store-operated calcium channels (SOC)^[3].

In vitro, QNZ (EVP4593) (10 μ M) treatment of mouse fibroblasts for 48h inhibited the proliferation and migration of fibroblasts and the expression of the proliferation marker Ki67 in cells^[4]. QNZ (EVP4593) (10 nM) treatment of LNCap and PC-3 cells for 7 days significantly increased the sensitivity of cells to carboplatin, inhibited the phosphorylation of intracellular AKT or p65, and increased the expression of E-cadherin^[5].

In vivo, QNZ (EVP4593) (1mg/kg) was administered intraperitoneally to rats with myocardial ischemia/reperfusion (I/R) injury, enhancing the cardioprotective effect induced by morphine postconditioning (MP) and attenuating myocardial ischemia/reperfusion injury^[6]. QNZ (EVP4593) (1mg/kg) was administered intraperitoneally to mice bearing DLD1 cell xenografts for 14 days, enhancing the antitumor activity of bevacizumab in vivo^[7].

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References:

- [1] Grekhnev D A, Kruchinina A A, Vigont V A, et al. The Mystery of EVP4593: Perspectives of the quinazoline-derived compound in the treatment of Huntington's disease and other human pathologies[J]. International Journal of Molecular Sciences, 2022, 23(24): 15724.
- [2] Tobe M, Isobe Y, Tomizawa H, et al. Discovery of quinazolines as a novel structural class of potent inhibitors of NF- κ B activation[J]. Bioorganic & medicinal chemistry, 2003, 11(3): 383-391.
- [3] Chauvet S, Jarvis L, Chevallet M, et al. Pharmacological characterization of the native store-operated calcium channels of cortical neurons from embryonic mouse brain[J]. Frontiers in pharmacology, 2016, 7: 486.
- [4] Huang F, Wang H, Zhang Y, et al. Synergistic effect of QNZ, an inhibitor of NF- κ B signaling, and bone morphogenetic protein 2 on osteogenic differentiation in mesenchymal stem cells through fibroblast-induced yes-associated protein activation[J]. International Journal of Molecular Sciences, 2023, 24(9): 7707.
- [5] He Y, Zhang Q, Chen H, et al. Astragaloside IV enhanced carboplatin sensitivity in prostate cancer by suppressing AKT/NF- κ B signaling pathway[J]. Biochemistry and Cell Biology, 2021, 99(2): 214-222.
- [6] Tu R H, Wang D X, Zhong G Q, et al. New targets of morphine postconditioning protection of the myocardium in ischemia/reperfusion injury: Involvement of HSP90/Akt and C5a/NF- κ B[J]. Open Medicine, 2021, 16(1): 1552-1563.
- [7] Marciano R, Prasad M, levy T, et al. High-throughput screening identified compounds sensitizing tumor cells to glucose starvation in culture and VEGF inhibitors in vivo[J]. Cancers, 2019, 11(2): 156.

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