

Product Data Sheet

Product Name: CCT020312

Cat. No.: GC33006

Chemical Properties

Cas. No. 324759-76-4

SMILES O=C1NC2=C(C(C3=CC=CC=C3)=C1C4=NN(C(C4)C5=CC=C(C=C5)Br)C(CCN(CC)CC)=O)C=C(C=C2)Br

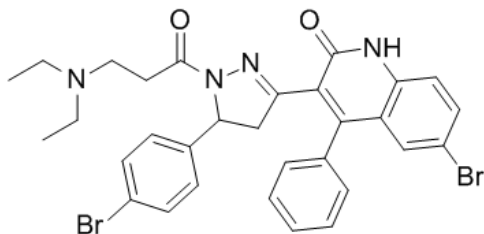
Formula $C_{31}H_{30}Br_2N_4O_2$ M.Wt 650.4

Solubility DMSO : 125 mg/mL (192.19 mM); Water : < 0.1 mg/mL (insoluble) 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 MDA-MB-453 and CAL-148 cells

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

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Preparation Method MDA-MB-453 (8×10^3 cells/well) and CAL-148 cells (4×10^3 cells/well) were seeded in 96-well plates and treated with CCT020312 at different doses for 24 or 48h. Then, 10 μ l of CCK-8 solution was added to each well and incubated for 1 or 2h at 37°C.

Reaction Conditions 2-12 μ M; 24h, 48h

Applications CCT020312 significantly inhibited cell viability in a dose-dependent manner.

Animal experiment [2]:

Animal models Inflammation-mediated osteoporosis (IMO) rat model

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Preparation Method	CCT020312 (CCT) was dissolved in 100μL sterile dimethyl sulfoxide (DMSO) and diluted by sterile normal saline to the density of 0.5mg/mL. Rats (n = 24) were randomly divided into four groups: Sham group, IMO group, IMO + 1mg/kg CCT group and IMO + 2mg/kg CCT group, with 6 rats in each group. All rats except for those in the Sham group were made into IMO models by bilateral ovariectomy (OVX) and magnesium silicate (Talc) injection. In brief, rats were anesthetized with an intraperitoneal injection of pentobarbital sodium (20mg/kg), OVX operation was performed (1st day), and metamizole sodium (25mg/kg) was administered to rats for two consecutive days. Sham rats did not receive OVX operation and only a little fatty tissue around the ovary was resected. On the 59th day after OVX operation, which allowed for osteoporosis to develop in the OVX rats, inflammation was induced by subcutaneously injected with Talc (magnesium silicate: 3.2 g in total per animal) in sterile saline in the back of the rats. Meanwhile, only the rats in the Sham group were subcutaneously injected with saline. From the 60th day on, rats were given with intraperitoneal injection (i.p.) of DMSO (vehicle control) or CCT (1mg/kg/day and 2mg/kg/day). Then, the rats were sacrificed through an overdose of thiopental sodium (50mg/kg) on the 80th day.
Dosage form	1mg/kg, 2mg/kg; ip; 20d
Applications	CCT020312 significantly alleviated the osteoporosis symptoms of IMO rats by improving bone remodeling indicators, increasing bone density, promoting osteogenesis, and inhibiting bone resorption and inflammation.

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References:

- [1]. Li X, Yu X, Zhou D, et al. CCT020312 inhibits triple-negative breast cancer through PERK pathway-mediated G1 phase cell cycle arrest and apoptosis. *Frontiers in Pharmacology*. 2020 May 19; 11: 737.
- [2]. Tang BM, Li ZW, Wang ZY. PERK activator CCT020312 prevents inflammation-mediated osteoporosis in the ovariectomized rats. *Gynecological Endocrinology*. 2021 Apr 3; 37(4): 342-348.

Background

CCT020312 is a selective protein kinase R-like endoplasmic reticulum kinase (PERK) pathway agonist [1]. CCT020312 activates the endoplasmic reticulum stress (ER stress)-related unfolded protein response (UPR) pathway by promoting eIF2 α phosphorylation and upregulating ATF4 expression, thereby inducing cell cycle arrest and autophagy [2-3]. CCT020312 is often used to study diseases such as tumors and neurodegenerative diseases [4].

In MDA-MB-453 and CAL-148 cells, CCT020312 (2-12 μ M; 24h, 48h) significantly inhibited cell viability in a dose-dependent manner [5]. In HT29 cells, CCT020312 (1-9 μ M; 24h) treatment effectively inhibited cell proliferation [6]. In HCT116 and SW480 cells, CCT020312 (0.625-50 μ M; 12h, 24h, 48h) exposure reduced the cell viability of cell in a time- and dose-dependent manner [7].

In inflammation-mediated osteoporosis (IMO) rat model, CCT020312 (1mg/kg, 2mg/kg; ip; 20d) significantly alleviated the osteoporosis symptoms of IMO rats by improving bone remodeling indicators, increasing bone density, promoting osteogenesis, and inhibiting bone resorption and inflammation [8]. In aged mice, activation of PERK with CCT020312 (2mg/kg; ip; single injection) increases the amount of GluN2A and GluN2B in synaptosomal preparations [9].

References:

- [1]. Bruch J, Xu H, Rösler TW, et al. PERK activation mitigates tau pathology in vitro and in vivo. *EMBO molecular medicine*. 2017 Mar; 9(3): 371-384.
- [2]. Stockwell SR, Platt G, Barrie SE, et al. Mechanism-based screen for G1/S checkpoint activators identifies a selective activator of EIF2AK3/PERK signalling. *PloS one*. 2012 Jan 12; 7(1): e28568.
- [3]. Zhou D, Yin M, Kang B, et al. CCT020312 exerts anti-prostate cancer effect by inducing G1 cell

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cycle arrest, apoptosis and autophagy through activation of PERK/eIF2 α /ATF4/CHOP signaling.

Biochemical pharmacology. 2024 Mar 1; 221: 116038.

[4]. Talukdar G, Orr HT, Lei Z. The PERK pathway: beneficial or detrimental for neurodegenerative diseases and tumor growth and cancer. Human molecular genetics. 2023 Aug 15; 32(16): 2545-2557.

[5]. Li X, Yu X, Zhou D, et al. CCT020312 inhibits triple-negative breast cancer through PERK pathway-mediated G1 phase cell cycle arrest and apoptosis. Frontiers in Pharmacology. 2020 May 19; 11: 737.

[6]. Stockwell SR, Platt G, Barrie SE, et al. Mechanism-based screen for G1/S checkpoint activators identifies a selective activator of EIF2AK3/PERK signalling. PloS one. 2012 Jan 12; 7(1): e28568.

[7]. Lei Y, He L, Yan C, et al. PERK activation by CCT020312 chemosensitizes colorectal cancer through inducing apoptosis regulated by ER stress. Biochemical and biophysical research communications. 2021 Jun 11; 557: 316-322.

[8]. Tang BM, Li ZW, Wang ZY. PERK activator CCT020312 prevents inflammation-mediated osteoporosis in the ovariectomized rats. Gynecological Endocrinology. 2021 Apr 3; 37(4): 342-348.

[9]. Chen K, Hu Q, Gupta R, et al. Inhibition of unfolded protein response prevents post-anesthesia neuronal hyperactivity and synapse loss in aged mice. Aging Cell. 2022 Apr; 21(4): e13592.

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