TBB

Cat. No.: HY-14394

CAS No.: 17374-26-4

Molecular Formula: $C_6HBr_4N_3$

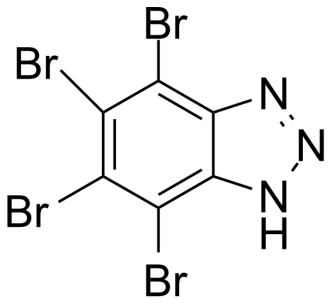
Molecular Weight: 434.71

Target: Casein Kinase

Pathway: Cell Cycle/DNA Damage; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (230.04 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3004 mL	11.5019 mL	23.0038 mL
5 mM	0.4601 mL	2.3004 mL	4.6008 mL
10 mM	0.2300 mL	1.1502 mL	2.3004 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.75 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.75 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.75 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TBB is a cell-permeable and ATP-competitive CK2 inhibitor with an IC_{50} of 0.15 μM for rat liver CK2.

IC_{50} & Target

CK2 0.15 μM (IC_{50}, Human CK2)	PIM1 1.04 μM (IC_{50})	PIM2 4.3 μM (IC_{50})	PIM3 0.86 μM (IC_{50})
HIPK2 5.3 μM (IC_{50})	HIPK3 4.9 μM (IC_{50})	DYRK1a 4.36 μM (IC_{50})	DYRK2 0.99 μM (IC_{50})

	DYRK3 5.3 μM (IC_{50})	PKD1 5.9 μM (IC_{50})	CDK2 14 μM (IC_{50})

In Vitro

Investigation of the inhibitory power of TBB with a panel of 33 protein kinases shows highest potency for CK2 (casein kinase 2) (human CK2: IC_{50}=1.6 μM at 100 μM ATP). TBB also inhibits three other kinases with less potency: CDK2 (IC_{50}=15.6 μM), phosphorylase kinase (IC_{50}=8.7 μM) and glycogen synthase kinase 3β (GSK3β) (IC_{50}=11.2 μM). All other kinases tested have IC50 values 50-fold greater than that for CK2[1]. The viability of the androgen insensitive PC-3 cells may be diminished by TBB (60 μM TBB) acting either alone or combined with anticancer agents CPT or TRAIL when a proper time schedule of the administration is applied. The time schedule-dependent activity of TBB does not come from its effect on apoptosis in PC-3 cells[2]. TBB is an ATP/GTP competitive inhibitor of protein kinase casein kinase-2 (CK2), has been examined against a panel of 33 protein kinases, either Ser/Thr- or Tyr-specific. In the presence of 10 μM TBB (and 100 μM ATP) only CK2 is drastically inhibited (>85%) whereas three kinases (phosphorylase kinase, glycogen synthase kinase 3L and cyclin-dependent kinase 2/cyclin A) underwent moderate inhibition, with IC_{50} values one-two orders of magnitude higher than CK2 (IC_{50}=0.9 μM). TBB also inhibits endogenous CK2 in cultured Jurkat cells[3].

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

In Vivo

The extent of retinal neovascularization in a mouse OIR model is reduced by approximately 60% after treatment with TBB (6 days at 60 mg/kg per day)[4].

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

PROTOCOL

Cell Assay [2]

PC-3 or HeLa cells are cultured routinely in RPMI-1640 and DMEM media, respectively, which are supplemented with 10% FBS, Penicillin (100 U/mL) and Streptomycin (100 μg/mL) at 37°C in a humidified atmosphere of 5% CO_2. Cells are seeded at 5×10^4 cells/well (PC-3) or 2×10^4 (HeLa) in 24-wells plates and cultured for 72 h. TBB (final concentration 60 μM), CPT (final concentration 5.8 nM), 2-deoxyglucose (2-DG; final concentration 0.5 mM) or TRAIL (final concentration 13.3 ng/mL) are added to the medium individually or in a combination and the cells are cultured for additional time, indicated on each figure. After treatment, the medium with the agent is removed and 500 μL of MTT mixture (0.5 mg/mL for PC-3 and 5.0 mg/mL for HeLa cells in medium without phenol red) is added to each well and incubated for an additional 1 h at 37°C. The formazan crystals are diluted in 250 μL of DMSO. The absorbance is measured at 570 nm[2].

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

Animal Administration [4]

Mice[4]

The heterozygous C57BL/6J mice are used. Emodin and TBB are injected intraperitoneally in volumes of 50 μL or less per mouse at doses of 15 to 30 mg/kg body weight, twice daily, starting from day 11. Control mice are injected with PEG-Tween vehicle alone.

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

CUSTOMER VALIDATION

- Redox Biol. 2021 Oct;46:102098.
- Cell Syst. 2018 Apr 25;6(4):424-443.e7.
- J Transl Med. 2022 Jul 21;20(1):325.
- Biochem Pharmacol. 2018 Feb;148:41-51.
- Epigenetics Chromatin. 2023 Apr 19;16(1):11.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. De Moliner E, et al. Alternative binding modes of an inhibitor to two different kinases. Eur J Biochem. 2003 Aug;270(15):3174-81.

[2]. Orzechowska E, et al. Time schedule-dependent effect of the CK2 inhibitor TBB on PC-3 human prostate cancer cell viability. Oncol Rep. 2012 Jan;27(1):281-5.

[3]. Sarno S, et al. Selectivity of 4,5,6,7-tetrabromobenzotriazole, an ATP site-directed inhibitor of protein kinase CK2 ('casein kinase-2'). FEBS Lett. 2001 May 4;496(1):44-8.

[4]. Ljubimov AV, et al. Involvement of protein kinase CK2 in angiogenesis and retinal neovascularization. Invest Ophthalmol Vis Sci. 2004 Dec;45(12):4583-91.

[5]. Pagano MA, et al. The selectivity of inhibitors of protein kinase CK2: an update. Biochem J. 2008 Nov 1;415(3):353-65.

[6]. Chen Z, et al. CK2α promotes advanced glycation end products-induced expressions of fibronectin and intercellular adhesion molecule-1 via activating MRTF-A in glomerular mesangial cells. Biochem Pharmacol. 2017 Dec 6;148:41-51.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

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