BCTC

Cat. No.: HY-19960

CAS No.: 393514-24-4

Molecular Formula: $C_{20}H_{25}ClN_4O$

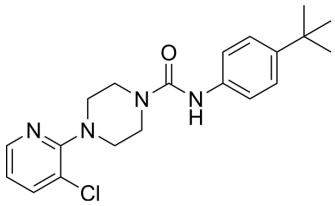
Molecular Weight: 372.89

Target: TRP Channel; Insulin Receptor; CGRP Receptor

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling; Protein Tyrosine Kinase/RTK; GPCR/G Protein

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 : ≥ 50 mg/mL (134.09 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6818 mL	13.4088 mL	26.8176 mL
5 mM	0.5364 mL	2.6818 mL	5.3635 mL
10 mM	0.2682 mL	1.3409 mL	2.6818 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.70 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.70 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BCTC is an orally active current inhibitor of vanilloid receptor type 1 (VR1). BCTC is a transient receptor potential cation channel subfamily M member 8 (TRPM8) and transient receptor potential vanilloid 1 (TRPV1) antagonist. BCTC is an insulin sensitizer and secretor. BCTC has anticancer and analgesic effects[1][2][3][4][5].

IC_{50} & Target

IC50: 37.0 nM (CGRP-LI)[3].
IC50: 36.0 nM (SP-LI)[3].

In Vitro

BCTC (20-100 μM; 72 h) shows highly selective antitumor activity in DU145 cells[1].

BCTC (20-100 μM; 48 h) induces cell cycle arrest in the G0/G1 phase by selectively regulating the expression levels of cell cycle regulatory protein subsets, and doesn't induce apoptosis[1].
BCTC (10 μM and 100 μM; 48 h) inhibits cell migration and invasion[1].
BCTC effectively inhibits the TRPV1 function of rat spinal cord by inhibiting the release of calcitonin gene-related peptide-like immunoreactivity (CGRP-LI) (IC_{50}=37.0 nM) and P-like substance immunoreactivity (SP-LI) (IC_{50}=36.0 nM) induced by capsaicin (300 nM) [3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	DU145
Concentration:	20 μM, 40 μM, 60 μM, 80 μM,100 μM
Incubation Time:	48 h
Result:	Down-regulated p-Akt, while p-GSK-3β was up-regulated leaving their unphosphorylated form unchanged. Significantly down-regulated Cyclin D1(20), the most relevant protein in the cell cycle, without affecting cyclin-B1. Reduced the expression of CDK2 and CDK6, but without affecting the expression level of CDK4. Downregulates MMP2 and p-FAK levels.

Cell Viability Assay[1]

Cell Line:	DU145, PNT1A
Concentration:	20 μM, 40 μM, 60 μM, 80 μM,100 μM
Incubation Time:	72 h
Result:	Decreased the growth of DU145 cells in a concentration-dependent manner, with 12.03% and 50.69% growth inhibition at 10 μM and 100 μM, respectively, but had little effect on normal prostate PNT1A cells.

In Vivo

BCTC (1-30 mg/kg; Oral gavage; Single dose) can inhibit inflammatory and neuropathic heat pain and mechanical hyperalgesia in Sprague-Dawley rats by targeting VR1, which has analgesic effect[2].
BCTC (10-100 mg/kg; Oral gavage, Twice daily for 4 weeks) improves the insulin resistance and systemic glucose and lipid metabolism, and increase insulin secretion in diabetic ob/ob mice[5].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Capsaicin-induced Sprague-Dawley rats model[2]
Dosage:	1 mg/kg, 3 mg/kg, 10 mg/kg, 30 mg/kg
Administration:	Oral gavage (p.o.), Single dose. Before capsaicin (HY-10448) treatment (30 μg; intraplantar injection; Single dose)
Result:	Inhibited capsaicin-mediated thermal hyperalgesia in a dose-dependent manner.

Animal Model:	Freund's complete adjuvant (FCA) Sprague-Dawley rats model[2]
Dosage:	1 mg/kg, 3 mg/kg, 10 mg/kg, 30 mg/kg
Administration:	Oral gavage (p.o.), Single dose. After 100 % FAC treatment (50 μL; intraplantar injection;

	Single dose)
Result:	Significantly reduced FAC-induced inflammation-related thermal pain and mechanical hyperalgesia, and extended the inhibitory effect of mechanical hyperalgesia to 6 h at high doses (10 mg/kg, 30 mg/kg).

Animal Model:	Partial sciatic nerve ligation Sprague-Dawley rats model[2]
Dosage:	1 mg/kg, 3 mg/kg, 10 mg/kg, 30 mg/kg
Administration:	Oral gavage (p.o.), Single dose. After partial sciatic nerve ligation.
Result:	Reduced post-operative abnormal tactile pain and mechanical hyperalgesia in a dose-dependent manner.

Animal Model:	Particularly strong insulin resistance and hyperinsulinemia ob/ob mice model[5]
Dosage:	10 mg/kg, 30 mg/kg, 100 mg/kg
Administration:	Oral gavage (p.o.); Twice daily for 4 weeks
Result:	Reduced plasma triglyceride and glucose area under the curve (AUC) level. Decreased calcitonin gene-related peptide (CGRP) levels in a dose-dependent manner.

CUSTOMER VALIDATION

- J Toxicol Sci. 2022;47(3):117-123.
- Fundam Toxicol Sci. 2023, 10(1): 1-6.

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REFERENCES

[1]. Liu T, et al. Anti-tumor activity of the TRPM8 inhibitor BCTC in prostate cancer DU145 cells. Oncol Lett. 2016 Jan;11(1):182-188.

[2]. Pomonis JD, et al. N-(4-Tertiarybutylphenyl)-4-(3-cholorphyridin-2-yl)tetrahydropyrazine -1(2H)-carbox-amide (BCTC), a novel, orally effective vanilloid receptor 1 antagonist with analgesic properties: II. in vivo characterization in rat models of inflammatory and neuropathic pain. J Pharmacol Exp Ther. 2003 Jul;306(1):387-93.

[3]. Kanai Y, et al. Involvement of an increased spinal TRPV1 sensitization through its up-regulation in mechanical allodynia of CCI rats. Neuropharmacology. 2005 Dec;49(7):977-84.

[4]. Nie C, et al. Study on chemical modification and analgesic activity of N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl) piperazine-1-carboxamide. Eur J Med Chem. 2020 May 15;194:112236.

[5]. Tanaka H, et al. Enhanced insulin secretion and sensitization in diabetic mice on chronic treatment with a transient receptor potential vanilloid 1 antagonist. Life Sci. 2011 Mar 14;88(11-12):559-63.

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

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