Product Data Sheet

Product Name: BOLD-100
Cat. No.: GC65318

Chemical Properties

Cas. No.	783324-98-1		
Formula	C14H12Cl4N4Ru	M.Wt	479.15
Solubility		Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	BOLD-100		

Protocol

Cell experiment [1]:

Cell lines	MCF7(2) cells (MCF7(2) is a MCF7 derivative cell line that shows increased sensitivity to estrogen)
Preparation Method	Cells were grown at 70% confluence on 100mm in complete growth medium for 24h. The following day, cells were treated with vehicle or 100μM BOLD-100 for an additional 72h. Cells were then fixed in ethanol, and analyzed by the Flow Cytometry. Each experiment was repeated at least three times.
Reaction Conditions	100μM; 72h

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Applications	Treatment of MCF7(2) cells with BOLD-100 significantly reduced the S phase and increased the G2/M phase compared with cells treated with the vehicle.

Animal experiment [2]:

Animal models	Balb/c SCID mice
Preparation Method	Hep3B xenografts were grown in Balb/c SCID mice and treated with BOLD-100 (30mg/kg; i.v.; once a week) and/or Sorafenib (25mg/kg; orally; five days a week) for 2 weeks when tumor nodules reached an average size of 25mm^3. Tumour size was assessed by caliper measurement.
Dosage form	30mg/kg; once a week for 2 weeks; i.v.
Applications	Withregardto the anticancer activity, BOLD-100 as well as Sorafenib monotreatment induced a distinct delay in tumour growth.

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References:
[1]Bakewell S, Conde I, Fallah Y, et al. Inhibition of DNA repair pathways and induction of ROS are potential mechanisms of action of the small molecule inhibitor BOLD-100 in breast cancer[J]. Cancers, 2020, 12(9): 2647.
[2]Heffeter P, Atil B, Kryeziu K, et al. The ruthenium compound KP1339 potentiates the anticancer activity of sorafenib in vitro and in vivo[J]. European Journal of Cancer, 2013, 49(15): 3366-3375.

Background

BOLD-100 is a ruthenium-based anticancer agent[1]. BOLD-100 has high tumor targeting potential, strongly binds to serum proteins such as albumin and transferrin, and is activated in the reducing tumor environment[2]. BOLD-100 can disrupt endoplasmic reticulum (ER) homeostasis and induce ER stress and unfolded protein response (UPR)[3].

In vitro, BOLD-100 (100μM) treatment of MCF7(2) cells for 72h significantly reduced S phase cells, increased G2/M phase cells, significantly reduced cell cycle proteins (such as RAD51, PCNA, ATM), and induced an increase in intracellular reactive oxygen species (ROS)[4]. BOLD-100 (100μM) treatment of HCT116 cells for 24h enhanced the phosphorylation of eIF2A serine 51 in cells, but reduced the expression of the basal ER chaperone GRP78[5]. BOLD-100 (0-200μM) has a significant inhibitory effect on malignant cell lines from various sources, such as liver cancer, melanoma, lung cancer and colon cancer, when treated for 72h, with an IC_{50} value of 45-200μM[6].

In vivo, BOLD-100 (30mg/kg) was treated by intravenous injection for 2 weeks in mice

with Hep3B cell xenografts, which significantly inhibited the growth of transplanted tumors in mice, improved the survival rate of mice, and increased the number of apoptotic cells in tumor tissues. It has a synergistic therapeutic effect with sorafenib[6]. BOLD-100 (50mg/kg) was treated by intravenous injection for 3 weeks in mice with VACO432 cell xenografts, but the inhibitory effect on tumor growth was not obvious. Combined treatment with AZD6738 can lead to a slowdown in tumor growth, but the tolerance is poor and the mice lose weight[7].

References:

[1] Swaminathan S, Haribabu J, Karvembu R. From Concept to Cure: The Road Ahead for Ruthenium-Based Anticancer Drugs[J]. ChemMedChem, 2024, 19(23): e202400435.
[2] Happl B, Brandt M, Balber T, et al. Synthesis and Preclinical Evaluation of Radiolabeled [103Ru] BOLD-100[J]. Pharmaceutics, 2023, 15(11): 2626.
[3] Ranzato E, Bonsignore G, Martinotti S. ER stress response and induction of apoptosis in malignant pleural mesothelioma: The Achilles heel targeted by the anticancer ruthenium drug BOLD-100[J]. Cancers, 2022, 14(17): 4126.
[4] Bakewell S, Conde I, Fallah Y, et al. Inhibition of DNA repair pathways and induction of ROS are potential mechanisms of action of the small molecule inhibitor BOLD-100 in breast cancer[J]. Cancers, 2020, 12(9): 2647.
[5] Baier D, Schoenhacker-Alte B, Rusz M, et al. The anticancer ruthenium compound BOLD-100 targets glycolysis and generates a metabolic vulnerability towards glucose deprivation[J]. Pharmaceutics, 2022, 14(2): 238.
[6] Heffeter P, Atil B, Kryeziu K, et al. The ruthenium compound KP1339 potentiates the anticancer activity of sorafenib in vitro and in vivo[J]. European Journal of Cancer, 2013, 49(15): 3366-3375.
[7] Griffin D, Carson R, Moss D, et al. Ruthenium Drug BOLD-100 Regulates BRAF MT Colorectal Cancer Cell Apoptosis through AhR/ROS/ATR Signaling Axis Modulation[J]. Molecular Cancer Research, 2024, 22(12): 1088-1101.

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