# Product Data Sheet

Product Name: VBIT-12
Cat. No.: GC39458

## Chemical Properties

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|---|---|---|---|
| Cas. No. | 2089227-65-4 | | |
| SMILES | O=C(O)CNC(C1(NC2=CC=CC=C2)CCN(CC3=C4C=CC=CC4=CC=C3)CC1)=O | | |
| Formula | $C_{25}H_{27}N_3O_3$ | M.Wt | 417.5 |
| Solubility | DMSO: 250 mg/mL (598.80 mM) | 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 | VBIT-12 | | |

## Protocol

### Cell experiment [1]:

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| Cell lines | Colon cells |
| Preparation Method | Cells (60% confluence) were incubated for 48h in a serum-free growth medium with different concentrations of DSS (dissolved in culture media and filter-sterilized using a 0.45μm filter) in triplicates. Cells were treated with different concentrations of DSS (1%–3%) in the absence or presence of VBIT-12 and analyzed for cell viability, VDAC1 expression levels, VDAC1 oligomerization, ROS production, mtDNA release, and apoptosis. |
| Reaction Conditions | 10μM, 20μM; 48h |


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| Applications | VBIT-12 treatment of cultured colon cells inhibits DSS-induced VDAC1 overexpression, oligomerization, and apoptosis. |

**Animal experiment [2]:**

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| Animal models | $SOD1^{G93A}$ transgenic mice |
| Preparation Method | For intraperitoneal (IP) injection, VBIT-12 (80mg/mL) in DMSO was diluted with saline, pH 7.0, to a final concentration of 3.25mg/mL. $SOD1^{G93A}$ transgenic mice received 200μL by IP injection resulting in a final VBIT-12 concentration of ~26mg/kg. VBIT-12 was IP injected every second day starting from day 60 for 12 weeks, and then the VBIT-12 final concentration was reduced to ~13mg/kg. The control group was IP injected with around 200μL of DMSO (4%). |
| Dosage form | 13mg/kg, 26mg/kg; ip; 12 weeks |
| Applications | $SOD1^{G93A}$ transgenic mice receiving intraperitoneal injection of VBIT-12 maintained limb muscle strength for a longer period of time. |


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References:
[1]. Verma A, Pittala S, Alhozeel B, et al. The role of the mitochondrial protein VDAC1 in inflammatory bowel disease: a potential therapeutic target. Molecular Therapy. 2022 Feb 2; 30(2): 726-744.
[2]. Shteinfer-Kuzmine A, Argueti-Ostrovsky S, Leyton-Jaimes MF, et al. Targeting the mitochondrial protein VDAC1 as a potential therapeutic strategy in ALS. International Journal of Molecular Sciences. 2022 Sep 1; 23(17): 9946.

## Background

VBIT-12 is a unique inhibitory protein for VDAC1 [1]. VBIT-12 induces VDAC1 binding, inhibits and promotes decay protein interaction, and inhibits granular membrane voltage potential and decreases cellular pigment C release, leading to anti-decay action [2]. VBIT-12 is commonly used to treat inflammation and cardiovascular diseases [3-4].

In colon cells, VBIT-12 (10μM, 20μM; 48h) treatment of cultured colon cells inhibit DSS-induced VDAC1 overexpression, oligomerization, and apoptosis [5]. In murine hepatocytes, VBIT-12 (20μM; 2h) protects mitochondria and alleviates APAP-induced ferroptosis [6]. In R28 retinal neuron-like cells, VBIT-12 (40μM; 2h) inhibits OGD/R-induced mitochondrial damage and attenuates cell death [7].

In $SOD1^{G93A}$ transgenic mice, receiving intraperitoneal injection of VBIT-12 (13mg/kg,

26mg/kg; ip; 12 weeks) maintained limb muscle strength for a longer period of time [8]. In 5×FAD transgenic mice, VBIT-12 (20mg/kg; po; 5 months) inhibits cognitive decline in mice [9]. In the caerulein hyperstimulation-induced pancreatitis mice model (CER), prophylactic administration of VBIT-12 (20mg/kg; po; 24h) attenuated pancreatic histological damage, significantly reduced VDAC1 oligomerization, and decreased serum amylase levels and pancreatic trypsin activity [10].

References:

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[2]. Magri A, Cubisino SA, Battiato G, et al. VDAC1 knockout affects mitochondrial oxygen consumption triggering a rearrangement of ETC by impacting on complex I activity. International Journal of Molecular Sciences. 2023 Feb 12; 24(4): 3687.
[3]. Shoshan-Barmatz V, Anand U, Nahon-Crystal E, et al. Adverse effects of metformin from diabetes to COVID-19, cancer, neurodegenerative diseases, and aging: is VDAC1 a common target?. Frontiers in physiology. 2021 Oct 4; 12: 730048.
[4]. Song JQ, Shen LJ, Wang HJ, et al. Discovery of Balasubramide Derivative with Tissue-Specific Anti-Inflammatory Activity Against Acute Lung Injury by Targeting VDAC1. Advanced Science. 2024 Dec;11(48): 2410550.
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[6]. Niu B, Lei X, Xu Q, et al. Protecting mitochondria via inhibiting VDAC1 oligomerization alleviates ferroptosis in acetaminophen-induced acute liver injury. Cell biology and toxicology. 2022 Jun 1: 1-26.
[7]. Wan H, Yan YD, Hu XM, et al. Inhibition of mitochondrial VDAC1 oligomerization alleviates apoptosis and necroptosis of retinal neurons following OGD/R injury. Annals of Anatomy-Anatomischer Anzeiger. 2023 Apr 1; 247: 152049.
[8]. Shteinfer-Kuzmine A, Argueti-Ostrovsky S, Leyton-Jaimes MF, et al. Targeting the mitochondrial protein VDAC1 as a potential therapeutic strategy in ALS. International Journal of Molecular Sciences. 2022 Sep 1; 23(17): 9946.
[9]. Verma A, Shteinfer-Kuzmine A, Kamenetsky N, et al. Targeting the overexpressed mitochondrial protein VDAC1 in a mouse model of Alzheimer’s disease protects against mitochondrial dysfunction and mitigates brain pathology. Translational

Neurodegeneration. 2022 Dec 28; 11(1): 58.
[10]. Chanda D, Thoudam T, Sinam IS, et al. Upregulation of the ERRγ–VDAC1 axis underlies the molecular pathogenesis of pancreatitis. Proceedings of the National Academy of Sciences. 2023 May 16; 120(20): e2219644120.