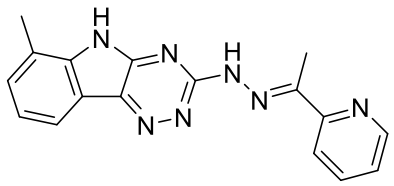
Product data sheet

MedKoo Cat#: 408097 Name: VLX600 CAS#: 327031-55-0 (free base) Chemical Formula: $C_{17}H_{15}N_7$ Exact Mass: 317.1389 Molecular Weight: 317.356	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
VLX600 is a Iron Chelator that Target Both Proliferating and Quiescent Cancer Cells. VLX600 potentiated the effect of radiation in tumor spheroids in a synergistic manner. VLX600 is a lipophilic cation-based triazinoindolyl-hydrazone compound and mitochondrial oxidative phosphorylation (OxPhos) inhibitor, with potential antineoplastic activity. Upon infusion, in normal cells and proliferating tumor cells where glucose is readily available,

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	19.0	59.87

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.15 mL	15.76 mL	31.51 mL
5 mM	0.63 mL	3.15 mL	6.30 mL
10 mM	0.32 mL	1.58 mL	3.15 mL
50 mM	0.06 mL	0.32 mL	0.63 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Karlsson H, Senkowski W, Fryknäs M, Mansoori S, Linder S, Gullbo J, Larsson R, Nygren P. A novel tumor spheroid model identifies selective enhancement of radiation by an inhibitor of oxidative phosphorylation. Oncotarget. 2019 Sep 3;10(51):5372-5382. doi: 10.18632/oncotarget.27166. PMID: 31523395; PMCID: PMC6731106.
2. Fryknäs M, Zhang X, Bremberg U, Senkowski W, Olofsson MH, Brandt P, Persson I, D'Arcy P, Gullbo J, Nygren P, Schughart LK, Linder S, Larsson R. Iron chelators target both proliferating and quiescent cancer cells. Sci Rep. 2016 Dec 7;6:38343. doi: 10.1038/srep38343. PMID: 27924826; PMCID: PMC5141479.

In vivo study

1. Karlsson H, Senkowski W, Fryknäs M, Mansoori S, Linder S, Gullbo J, Larsson R, Nygren P. A novel tumor spheroid model identifies selective enhancement of radiation by an inhibitor of oxidative phosphorylation. Oncotarget. 2019 Sep 3;10(51):5372-5382. doi: 10.18632/oncotarget.27166. PMID: 31523395; PMCID: PMC6731106.
2. Zhang X, Fryknäs M, Hernlund E, Fayad W, De Milito A, Olofsson MH, Gogvadze V, Dang L, Påhlman S, Schughart LA, Rickardson L, D'Arcy P, Gullbo J, Nygren P, Larsson R, Linder S. Induction of mitochondrial dysfunction as a strategy for targeting tumour cells in metabolically compromised microenvironments. Nat Commun. 2014;5:3295. doi: 10.1038/ncomms4295. PMID: 24548894; PMCID: PMC3929804.

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7. Bioactivity

Biological target:

VLX600 is an iron-chelating inhibitor of oxidative phosphorylation (OXPHOS) that causes mitochondrial dysfunction and induces a strong shift to glycolysis.

In vitro activity

VLX600 was identified in a screen for compounds active on 3-D tumor spheroids but also shows antiproliferative activity on colon cancer cell lines in monolayer culture. The effect of VLX600 was examined on a number of colon cancer cell lines and generally found IC50 values in the order of 1 μM (Fig. 3A–G). VLX600 was more potent than other iron chelators (i.e. Triapine (3-aminopyridine-2-carboxaldehyde-thiosemicarbazone), CPX, VLX5019, and deferoxamine) (Fig. 3A–G). DNA synthesis of colon cancer cells grown in monolayer culture was inhibited as evidenced by decreased incorporation of 5-ethynyl-2′ -deoxyuridine (EdU) (Fig. 3H,I). The catalytic activity of ribonucleotide reductase is dependent on an iron-binding site in the M2 subunit of the enzyme and iron chelators have been found to inhibit this enzyme20. As expected, VLX600 inhibited ribonucleotide reductase activity in vitro (Fig. 3J).

Reference: Sci Rep. 2016; 6: 38343. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5141479/

In vivo activity

To study the effects of VLX600 in vivo, the drug was injected intravenously in NMRI mice. The compound was rapidly distributed and finally eliminated with a half-life of ~4–5 h. Using the maximally tolerated dose, antitumour activity was observed in both HCT116 and HT29 colon cancer xenografts (Fig. 7b–e). Importantly, minimal systemic toxicity was observed as evidenced by no loss of body mass and no or minor changes in plasma parameters such as liver alanine aminotransferase, blood glucose and total protein (Supplementary Fig. 7a,b). Sections from VLX600-treated HCT116 tumours were examined. VLX600 treatment resulted in a decreased Ki67-labelling index (Fig. 7f) consistent with growth arrest. Large cytoplasmic vesicles were also observed (Fig. 7g), suggesting that the compound induced the formation of autolysosomes also in vivo. On the basis of the results of this study, a model for the effect of VLX600 on normal and tumour cells in different microenvironments is presented in Fig. 8.

Reference: Nat Commun. 2014 Feb 18; 5: 3295. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3929804/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.