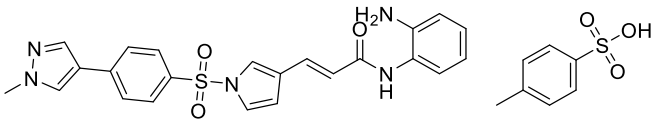
Product data sheet

MedKoo Cat#: 205800 Name: 4SC-202 CAS#: 910462-43-0 Chemical Formula: $C_{23}H_{21}N_5O_3S$ Exact Mass: 447.13651 Molecular Weight: 447.51	
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:

Domatinostat, also known as 4SC-202, is an orally bioavailable benzamide and inhibitor of human class I histone deacetylases (HDACs) isoenzymes 1, 2 and 3, with potential antineoplastic activity. HDAC inhibitor 4SC-202 selectively binds to and inhibits class I HDACs leading to an accumulation of highly acetylated histones. This may result in an induction of chromatin remodeling, the selective transcription of tumor suppressor genes, and the tumor suppressor protein-mediated inhibition of tumor cell division and eventually the induction of tumor cell apoptosis. This may inhibit tumor cell proliferation in susceptible tumor cells. HDACs, upregulated in many tumor types, are a class of enzymes that deacetylate chromatin histone proteins.

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	89	198.88

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.23 mL	11.17 mL	22.35 mL
5 mM	0.45 mL	2.23 mL	4.47 mL
10 mM	0.22 mL	1.12 mL	2.23 mL
50 mM	0.04 mL	0.22 mL	0.45 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. Zhijun H, Shusheng W, Han M, Jianping L, Li-Sen Q, Dechun L. Pre-clinical characterization of 4SC-202, a novel class I HDAC inhibitor, against colorectal cancer cells. Tumour Biol. 2016 Aug;37(8):10257-67. doi: 10.1007/s13277-016-4868-6. Epub 2016 Feb 1. PMID: 26831668.

2. Fu M, Wan F, Li Z, Zhang F. 4SC-202 activates ASK1-dependent mitochondrial apoptosis pathway to inhibit hepatocellular carcinoma cells. Biochem Biophys Res Commun. 2016 Mar 4;471(2):267-73. doi: 10.1016/j.bbrc.2016.01.030. Epub 2016 Jan 8. PMID: 26773495.

In vivo study

1. Wang W, Zhang Z, Kuang X, Ma D, Xiong J, Lu T, Zhang Y, Yu K, Zhang S, Wang J, Fang Q. 4SC-202 induces apoptosis in myelodysplastic syndromes and the underlying mechanism. Am J Transl Res. 2020 Jun 15;12(6):2968-2983. PMID: 32655823; PMCID: PMC7344078.

Product data sheet

7. Bioactivity

Biological target:

Domatinostat (4SC-202) is a selective class I HDAC inhibitor with IC50 of 1.20 μM, 1.12 μM, and 0.57 μM for HDAC1, HDAC2, and HDAC3, respectively. Also displays inhibitory activity against Lysine specific demethylase 1 (LSD1).

In vitro activity

Histone deacetylase (HDAC) overactivity in colorectal cancer (CRC) promotes cancer progression. In the current study, it was shown that 4SC-202 potently inhibited survival and proliferation of primary human colon cancer cells and established CRC lines (HT-29, HCT-116, HT-15, and DLD-1). Yet, the same 4SC-202 treatment was non-cytotoxic to colon epithelial cells where HDAC-1/-2 expressions were extremely low. 4SC-202 provoked apoptosis activation in CRC cells, while caspase inhibitors (z-VAD-CHO and z-DVED-CHO) significantly alleviated 4SC-202-exerted cytotoxicity in CRC cells. Meanwhile, 4SC-202 induced dramatic G2-M arrest in CRC cells. Further studies showed that AKT activation might be an important resistance factor of 4SC-202. 4SC-202-induced cytotoxicity was dramatically potentiated with serum starvation, AKT inhibition (by perifosine or MK-2206), or AKT1-shRNA knockdown in CRC cells. On the other hand, exogenous expression of constitutively active AKT1 (CA-AKT1) decreased the sensitivity by 4SC-202 in HT-29 cells.

Reference: Tumour Biol. 2016 Aug;37(8):10257-67. https://link.springer.com/article/10.1007/s13277-016-4868-6

In vivo activity

SKM-1 cells transfected with LV-HO-1 and its empty vector (EV) were injected to the tail vein of NOD/SCID mice. After confirming successful engraftment in these recipient mice at 14 days after transplantation, 4SC-202 was orally administered at a dose of 80 mg/kg/day for five consecutive days, followed by observation of the change in human CD45-positive cells by flow cytometry. As a result, after 2 weeks of 4SC-202 administration, the proportion of human CD34-positive cells were significantly decreased, and it was found that up-regulation of HO-1 accelerated cell proliferation and decreased the 4SC-202-inhibited MDS cell proliferation (Figure 5A, 5B). Meanwhile, observations were made for 130 days and recorded the death time of these mice, which was showed by aplan-Meier plot. The survival curve indicated that 4SC-202 effectively improved the survival of recipient mice, however, up-regulation of HO-1 delayed the time of 4SC-202-killing SKM-1 cells (Figure 5C). These results indicated that 4SC-202 effectively inhibited MDS cell proliferation and HO-1 influenced the inhibitory effects of 4SC-202 on SKM-1 cell proliferation in vivo.

Reference: Am J Transl Res. 2020 Jun 15;12(6):2968-2983. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/32655823/

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.