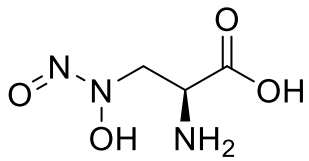
Product data sheet

MedKoo Cat#: 200130 Name: Alanosine CAS#: 5854-93-3 Chemical Formula: $C_3H_7N_3O_4$ Exact Mass: 149.0437 Molecular Weight: 149.11	
Product supplied as:	Powder
Purity (by HPLC):	≥ 90%
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:

Alanosine, also known as L-alanosine, is an amino acid analogue and antibiotic derived from the bacterium Streptomyces alanosinicus with antimetabolite and potential antineoplastic activities. L-alanosine inhibits adenylosuccinate synthetase, which converts inosine monophospate (IMP) into adenylosuccinate, an intermediate in purine metabolism. L-alanosine-induced disruption of de novo purine biosynthesis is potentiated by methylthioadenosine phosphorylase (MTAP) deficiency. The clinical use of this agent may be limited by its toxicity profile. MTAP is a key enzyme in the adenine and methionine salvage pathways.

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
Water	8.0	53.65
100 mM HCl	1.0	6.71
100 mM NaOH	1.0	6.71

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	6.71 mL	33.53 mL	67.06 mL
5 mM	1.34 mL	6.71 mL	13.41 mL
10 mM	0.67 mL	3.35 mL	6.71 mL
50 mM	0.13 mL	0.67 mL	1.34 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. Graff JC, Plagemann PG. Alanosine toxicity in Novikoff rat hepatoma cells due to inhibition of the conversion of inosine monophosphate to adenosine monophosphate. Cancer Res. 1976 Apr;36(4):1428-40. PMID: 177207.
2. Batova A, Diccianni MB, Omura-Minamisawa M, Yu J, Carrera CJ, Bridgeman LJ, Kung FH, Pullen J, Amylon MD, Yu AL. Use of alanosine as a methylthioadenosine phosphorylase-selective therapy for T-cell acute lymphoblastic leukemia in vitro. Cancer Res. 1999 Apr 1;59(7):1492-7. PMID: 10197619.

In vivo study

1. Li XM, Kanekal S, Crépin D, Guettier C, Carrière J, Elliott G, Lévi F. Circadian pharmacology of L-alanosine (SDX-102) in mice. Mol Cancer Ther. 2006 Feb;5(2):337-46. doi: 10.1158/1535-7163.MCT-05-0332. PMID: 16505107.

7. Bioactivity

Biological target: Adenylosuccinate synthetase inhibitor.

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In vitro activity

2-Amino-3-(hydroxynitrosoamino)propionic acid (alanosine), at a concentration as low as 2.7 muM, completely inhibits the incorporation of hypoxanthine into adenosine triphosphate by cultured Novikoff rat hepatoma cells. Alanosine inhibits the first step in the conversion of inosine monophosphate to adenosine monophosphate because inosine monophosphate, but not adenylosuccinate, accumulates in treated cells. Alanosine treatment results in the inhibition of cell division, DNA synthesis, RNA and protein synthesis (in this order), and a depletion of the cells of adenosine triphosphate. Some of the cells accumulate in late G2 or M, but the remainder become arrested in other stages of the cell cycle.

Reference: Cancer Res. 1976 Apr;36(4):1428-40. https://cancerres.aacrjournals.org/content/36/4/1428.long

In vivo activity

L-alanosine (SDX-102) exerts its cytotoxicity through inhibition of de novo purine biosynthesis, an effect potentiated by methylthioadenosine phosphorylase (MTAP) deficiency. The relevance of circadian dosing time was investigated for chronotherapeutic optimization of SDX-102. Toxicity was assessed in healthy mice following single (1,150, 1,650, or 1,850 mg/kg/d) or multiple doses (250 or 270 mg/kg/d). Efficacy was tested in mice with P388 leukemia receiving multiple doses (225 or 250 mg/kg/d). SDX-102 was administered at six circadian times 4 hours apart in mice synchronized with 12 hours of light alternating with 12 hours of darkness. MTAP expression was determined in liver, bone marrow, small intestinal mucosa, and P388 cells. Dosing at 19 hours after light onset reduced lethality 5-fold after single administration and 3-fold after multiple doses as compared with worst time [$P < 0.001$ and $P < 0.01$, respectively (chi2 test)]. Neutropenia, lymphopenia, and bone marrow hemorrhagic lesions were significantly less in mice dosed at 19 hours after light onset as compared with 7 hours after light onset. SDX-102 at 7 hours after light onset transiently ablated the 24-hour patterns in body temperature and activity. A circadian rhythm characterized small intestinal MTAP expression with a maximum at 6:30 hours after light onset ($P = 0.04$). A minor survival improvement was found in MTAP-deficient P388 mice receiving SDX-102 at 7 or 23 hours after light onset as compared with other times ($P = 0.03$, log-rank test). In conclusion, the therapeutic index of SDX-102 was improved by the delivery of SDX-102 in the mid to late activity span.

Reference: Mol Cancer Ther. 2006 Feb;5(2):337-46. https://mct.aacrjournals.org/content/5/2/337.long