

Product Data Sheet

Product Name: AICAR
Cat. No.: GC10518

Chemical Properties

Cas. No. 2627-69-2

Chemical Name 5-amino-1-[(2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]imidazole-4-carboxamide

SMILES CC(C=C(C)C=CC(=O)NO)C(=O)C1=CC=C(C=C1)N(C)C

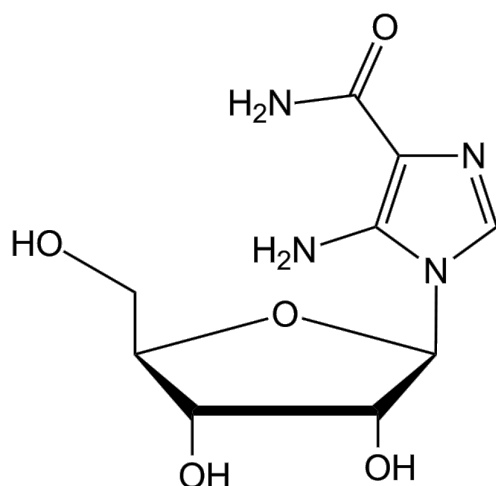
Formula $C_9H_{14}N_4O_5$ M.Wt 258.23

Solubility ≥ 12.9 mg/mL in DMSO, ≥ 52.9 mg/mL in Water Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C 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



Protocol

Cell experiment [1]:

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell lines	Nine human MCL cell lines (GRANTA-519, JVM-2, JEKO-1, Z-138, MAVER-1, REC-1, UPN-1, HBL-2 and MINO)
Preparation Method	MCL cell lines were incubated with AICAR at doses ranging from 0.1 to 2 mM for 24 or 48 hours.
Reaction Conditions	0.1 to 2 mM for 24 or 48 hours.
Applications	Most of the cell lines analyzed (REC-1, JEKO-1, UPN-1, JVM-2, MAVER-1 and Z-138) showed a IC50 lower than 1 mM after 48 hours of acadesine incubation.
Animal experiment [2]:	
Animal models	Female Nude NMRI Mice
Preparation Method	Mice were randomized into two experimental groups, each containing 15 animals. Animals in both groups received a 100 µl injection of 5*10 ⁶ K562 leukemia cells on both flanks. When tumors reached 150-200 mm ³ , animals were injected intraperitoneally with NaCl 0.9% or AICAR at dose level of 50 mg/kg body weight.
Dosage form	Intraperitoneal injection, 0, 0.25, 0.5, 1 or 2 mg
Applications	AICAR significantly reduced tumor formation in nude mice. Statistical analysis of tumor size shows a robust reduction of 68% at day 16 and 51% at day 20.

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References:

- [1]: Montraveta A, Xargay-Torrent S, LÓpez-Guerra M, et al. Synergistic anti-tumor activity of acadesine (AICAR) in combination with the anti-CD20 monoclonal antibody rituximab in in vivo and in vitro models of mantle cell lymphoma[J]. Oncotarget, 2014, 5(3): 726.
- [2]: Robert G, Ben Sahra I, Puissant A, et al. Acadesine kills chronic myelogenous leukemia (CML) cells through PKC-dependent induction of autophagic cell death[J]. PloS one, 2009, 4(11): e7889.

Background

AICAR (also called acadesine) is a purine nucleoside. Three pharmacological applications of AICAR were identified: i) stimulation under ischemic conditions of the cardiac production of the vasodilator, adenosine [1]; ii) inhibition of hepatic gluconeogenesis at the level of fructose-1,6-bisphosphatase [2], of therapeutic potential in diabetes; and iii) stimulation of AMP-activated protein kinase (AMPK), initially applied to inhibit the hepatic synthesis of triglycerides and cholesterol [3].

AICAR (treated 48 hours) inhibited cell proliferation of mantle cell lymphoma (MCL) cell lines, REC-1, JEKO-1, UPN-1, JVM-2, MAVER-1 and Z-138, with IC50s of 0.28, 0.59, 0.64, 0.98, 0.50, and 0.14 Mm respectively [4]. AICAR inhibited the growth and depletion of pyrimidine nucleotide pools in fibroblasts [5], accelerated repletion of purine nucleotide pools in heart [6], inhibition of fatty acid, sterol synthesis, and gluconeogenesis in hepatocytes, and increase in glucose uptake in muscle [7].

AICAR (500 mg/kg) injected intraperitoneally into C57BL/6J mice 1 hour before LPS administration. LPS induced the expression of TF mRNA in many major organs, including the lung and liver [8]. A daily administration of 400mg/kg AICAR in mice previously inoculated with a MCL xenotransplant significantly reduced tumor burden when compared to control animals, as soon as 7 days of treatment [9].

References:

- [1]. Gruber H E, Hoffer M E, McAllister D R, et al. Increased adenosine concentration in blood from ischemic myocardium by AICA riboside. Effects on flow, granulocytes, and injury[J]. Circulation, 1989, 80(5): 1400-1411.
- [2]. Vincent M F, Marangos P J, Gruber H E, et al. Inhibition by AICA riboside of gluconeogenesis in isolated rat hepatocytes[J]. Diabetes, 1991, 40(10): 1259-1266.

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- [3]. Hardie D G, Carling D, Carlson M. The AMP-activated/SNF1 protein kinase subfamily: metabolic sensors of the eukaryotic cell?[J]. Annual review of biochemistry, 1998, 67: 821.
- [4]. Montraveta A, Xargay-Torrent S, López-Guerra M, et al. Synergistic anti-tumor activity of acadesine (AICAR) in combination with the anti-CD20 monoclonal antibody rituximab in in vivo and in vitro models of mantle cell lymphoma[J]. Oncotarget, 2014, 5(3): 726.
- [5]. Sabina R L, Patterson D, Holmes E W. 5-Amino-4-imidazolecarboxamide riboside (Z-ribose) metabolism in eukaryotic cells[J]. Journal of Biological Chemistry, 1985, 260(10): 6107-6114.
- [6]. Swain J L, Hines J J, Sabina R L, et al. Accelerated repletion of ATP and GTP pools in postischemic canine myocardium using a precursor of purine de novo synthesis[J]. Circulation Research, 1982, 51(1): 102-105.
- [7]. Hardie D G, Carling D, Carlson M. The AMP-activated/SNF1 protein kinase subfamily: metabolic sensors of the eukaryotic cell?[J]. Annual review of biochemistry, 1998, 67: 821.
- [8]. Zhang W, Wang J, Wang H, et al. Acadesine inhibits tissue factor induction and thrombus formation by activating the phosphoinositide 3-kinase/Akt signaling pathway[J]. Arteriosclerosis, thrombosis, and vascular biology, 2010, 30(5): 1000-1006.
- [9]. Montraveta A, de Frias M, Campa's C, et al. The Nucleoside Analogue Acadesine Exerts Antitumoral Activity and Cooperates with Conventional Agents In In Vitro and In Vivo Models of Mantle Cell Lymphoma[J]. Blood, 2010, 116(21): 3918.

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