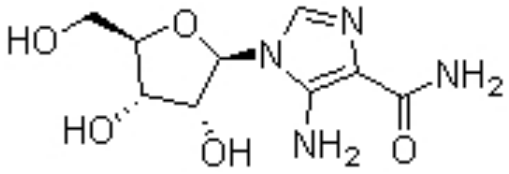
Product Introduction

Acadesine

Acadesine results in accumulation of ZMP, which mimics the stimulating effect of AMP on **AMPK** and **AMPK kinase**. Phase 3.

Technical Data:

Molecular Weight (MW):	258.23	
Formula:	$C_9H_{14}N_4O_5$	
Solubility (25°C) *** <1 mg/ml means slightly soluble or insoluble:**	DMSO 2 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	2627-69-2	

Biological Activity

Acadesine (500 μM) increases the ZMP content in extracts of isolated hepatocytes after up to 30-40 min treatment, then remains fairly constant at approximately 4 nmol/g. Acadesine (500 μM) causes a transient 12-fold activation of AMPK at 15 min in rat hepatocytes and 2-3 fold activation of AMPK in adipocytes, without affecting levels of ATP, ADP or AMP. Acadesine (500 μM) causes a dramatic inhibition of both fatty acid and sterol synthesis in rat hepatocytes. Acadesine (500 μM) also causes a dramatic inactivation of HMG-CoA reductase. [1] Acadesine induces apoptosis of B-CLL cells in a dose-dependent manner with

EC50 of 380 μM. Acadesine (0.5 mM) decreases cell viability of B-CLL cells from 20 representative patients from 68% to 26%. Acadesine (0.5 mM) induces caspase activation and cytochrome crelease from mitochondria. Uptake and phosphorylation of Acadesine (0.5 mM) are required to induce apoptosis and activate AMPK in B-CLL cells. Acadesine (2-4 mM) only slightly affects the viability of T cells from B-CLL patients, Acadesine (0.5 mM) remarkedly reduces viability of B cells but not T cells. [2] Acadesine triggers loss of cell metabolism in K562, LAMA-84 and JURL-MK1 and is also effective in killing imatinib-resistant K562 cells and Ba/F3 cells carrying the T315I-BCR-ABL mutation. The effect of Acadesine is abrogated by GF109203X and Ro-32-0432, both inhibitor of classical and new PKCs and accordingly, Acadesine triggers relocation and activation of several PKC isoforms in K562 cells. Acadesine dose-dependently inhibits K562 colony formation at day 10, the growth inhibitory effect of acadesine is already detected at 0.25 mM and is maximal at 2.5 mM. [3] Acadesine causes a concentration-related reduction in CD18 expression on LPS-stimulated neutrophils in vitro. [4] Acadesine significantly (1 mM) inhibits N-formyl-methionyl-leucyl-phenylalanine-induced granulocyte CD11b up-regulation by a mean of 61% in blood. [5]

Acadesine (50 mg/kg) significantly reduces tumor formation in a mouse xenograft model of K562 cells. [3] Acadesine (10 mg/kg) results in higher fluid required to stabilize hemodynamics in pigs. Acadesine (10 mg/kg) inhibits LPS-induced protein permeability of pulmonary capillaries, peak inspiratory pressures on constant tidal volume and dead space ventilation in pigs. [4]

A potential first-in-class adenosine regulating agent (ARA).

References

[1] Corton JM, et al. Eur J Biochem, 1995, 229(2), 558-565.

[2] Campàs C, et al. Blood, 2003, 101(9), 3674-368

[3] Robert G, et al. PLoS One, 2009, 4(11), e7889.

[4] Fabian TC, et al. Surgery, 1996, 119(3), 302-315.

[5] Mathew JP, et al. J Thorac Cardiovasc Surg, 1995, 109(3), 448-456.

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