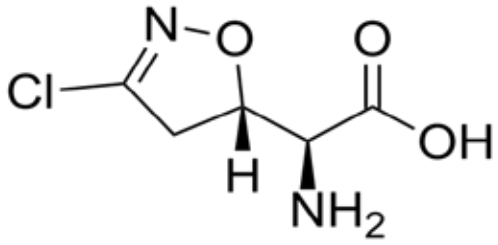
Acivicin

Acivicin (A0934) is a heterocyclic analog of L-glutamate originally produced by *Streptomyces sviceus*. Acivicin exhibits antimicrobial and anticancer activities.

Acivicin inhibits γ-glutamyltranspeptidase (γ-GT), an enzyme involved in transferring γ-glutamyl groups in the cell membranes of the kidneys, heart, brain, and pancreas. γ-GT moves amino acids across cell membranes and is important for homeostasis of oxidative stress. Acivicin covalently binds the active site of γ-GT, inducing a conformational change in which the C-terminal end folds to block entry and exit to the active site; this renders the enzyme incapable of catalyzing other reactions[1]. As glutathione is hydrolyzed by γ-GT, acivicin is often used to study glutathione homeostasis.

Acivicin inhibits glutamine amidotransferases such as GMP synthase and IGP synthase. Acivicin suppresses the growth of hepatoma cells in vitro, preventing the incorporation of uridine and thymidine into macromolecules and decreasing pools of CTP, GTP, dCTP, dGTP, and tTTP[2]. In this study, acivicin also inhibits CTP synthase. Other studies indicate depletion of all nucleoside triphosphate pools[3].



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Acivicin also exhibits chemotherapeutic activity in clinical trials, although potential benefit has been limited by CNS toxicity[4]. This compound has also been studied as a low-dose supplement to other chemotherapeutics such as cisplatin, as inhibition of γ-GT suppresses cisplatin-induced nephrotoxicity[5].

Acivicin's inhibition of GMP synthase also limits its pathogenicity of fungal microbes *Candida albicans* and *Aspergillus fumigatus*[6]. Analogs of acivicin are in various stages of development as antiparasitic compounds, owing to their increased affinity for CTP synthase[7].

References:
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